The Influence of Hemorrhage Upon Metabolism.

BY

Philip Bovier Hawk

[illegible] fulfilment of the requirements for the degree
of [illegible] of Philosophy in the Faculty of [illegible]
[illegible] Columbia University

The Influence of Hemorrhage Upon Metabolism.

BY

Philip Bovier Hawk.

Submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy in the Faculty of Pure Science, Columbia University.

1905.
The Chemical Publishing Co.,
Easton, Pa.

CONTENTS.

A.—HISTORICAL INTRODUCTION.

The practice of venesection, or blood-letting, is as old almost as the practice of medicine. History informs us that even as early as the time of Galen the employment of venesection was quite general. The withdrawal of blood was for many centuries looked upon as the most satisfactory remedy possessed by the practitioner, and indeed in a great number of diseases was considered to be the only means of preserving life. The mere question of the withdrawal of blood was never debated, the amount being the only question to decide, as it was almost universally taken for granted that some blood must be drawn. Galen himself employed blood-letting to the point of syncope, and his principal treatment for fever was blood-letting and the application of cold. So great was the faith in the "Universal treatment," as it came to be called, that its domain of influence was expanded and came to include the realms of religion and superstition. The desire to do evil was supposedly dissipated by its magic; and, if the venesection were carried out at the proper time, astrologically, such desirable possessions as a retentive memory, a strong mind, etc., were said to be acquired. The withdrawal of blood was accomplished by means of the leech, the cupping instrument, or by direct withdrawal from an opened vein (venesection), the individual conditions as well as the amount of blood to be drawn generally determining the method.

The universal practice of blood-letting has, however, long since passed, and although there are today certain diseased conditions in which loss of blood is supposed to possess curative power, the custom of blood-letting is practiced in much narrower limits than in the early centuries of its use. In the words of an eminent investigator "The waste of blood of a not very distant past is, let us hope, gone forever." To-day the greatest losses of blood with which we have to deal occur either as the result of accident, in major surgical operations, or in a few maladies, such as gastric ulcer, which are accompanied by internal bleeding.

The present investigation was undertaken with the accidental hemorrahge and the loss of blood incident to surgical procedure

especially in mind. The variations in the metabolic activity as indicated by the composition of the urine was the principal point of observation, and the changes in the chemical composition of the blood was a secondary consideration. No study of the form elements of the blood was made.

It is evident that a loss of blood from any organism will cause an alteration in the physical and chemical composition of the residual portion. It is further well understood that certain diseases are accompanied by changes in the blood. The nature of those alterations or changes (whether due directly to the reduction of the total blood or whether arising from an internal pathalogical state) and their effect upon the metabolic functions of the organism are questions of great interest and importance. It was but natural that a method of treatment holding undisputed sway for so many hundred years, as did that of blood-letting, should, with the growth of the spirit of investigation, be made the subject of many scientific observations. As would naturally follow, many of these observations were upon human subjects, while lower animals were the subject of other investigations. Observations of the first order were obviously almost entirely confined to diseased subjects. The field covered by investigations upon the effect of loss of blood as well as upon the influence of blood degeneration through pathalogical agencies is a field of great breadth, and while investigations of the second type cannot strictly be classed with our investigation, yet for a more complete survey of the entire subject we have included observations of that nature in our literary review.

The work of previous investigators may be divided into three general classes and corresponding sub-groups:

Class I. Observations upon the influence of the loss of blood as shown by direct experimentation upon lower animals.

1. Variations in the metabolic activities of the organism as shown by (a) Examination of the urine and determination of the body weight.
   (b) Respiratory exchange.
2. Alterations in the number of red corpuscles or percentage of haemoglobin.
3. Change in the number of leucocytes.

4. Influence on respiration, nervous system, and body temperature.
5. Changes in the fibrin content, specific gravity, coagulation rate, and in the composition of the blood, serum, gases, etc.

Class II. Observations upon the alterations in metabolic activity and in blood composition resulting, in human subjects, from internal pathalogical conditions, (anaemia, leukaemia, chlorosis, leucocytosis, etc).

Class III. Observations upon the influence of the loss of blood occurring pathalogically in human subjects, (gastric ulcer, duodenal ulcer, post-partum hemorrhage).

Our own investigation would be classified under groups 1 (a) and 5 of the first class.

Investigations having for their purpose the study of variations in the metabolic activities of the organism accompanying hemorrhage as shown by extensive urine analyses are comparatively few in number. The work of Bauer[1] is probably the most frequently quoted in this connection. His observations were upon well-nourished and fasting dogs, a single experiment being made upon each. A sheep hound weighing about 20kg. was the subject of the first form of experiment. This animal was fed a uniform daily diet until nitrogen equilibrium was attained, and was then subjected to a hemorrhage of 350-400 cc. of blood. Following this hemorrhage the variation in the proteid metabolism as shown by the nitrogen content of the urine was noted. The dog drank water "ad libitum." The urine of the preliminary period showed an average daily content of 16.6 grams of nitrogen. The hemorrhage caused an increased output of nitrogen and the daily average for the three days following was 20 grams, while the average for a period of five days was 18.9 grams. Thus the immediate effect of a loss of blood aggregating about 2% of the body weight of the animal was an increase of 10.2 grams of nitrogen in three days, and an increase of 11.5 grams in five days. From this point the rate of excretion of nitrogen fell rapidly, being slightly below normal at the end of the experiment. The volume of the urine increased somewhat after blood-letting, probably due to uncontrolled water ingestion, while the animal also gained slightly in body weight.

Experiments on a fasting dog were also followed by a rise in the urine volume and in the nitrogen content. From the data the author concluded that the influence of the loss of blood was much greater in the well-nourished organism than in the organism in the fasting condition.

As a "check" upon his results Bauer made three control experiments in which the customary operative steps were followed but no blood was drawn. These were on well-nourished dogs in a condition of nitrogen equilibrium and from them he concluded that the operation had no influence upon the execution of nitrogen by the urine.

Experiments along lines similar to those pursued by Bauer have been made by Jürgensen,[2] Maltschewsky,[3] and Ascoli and Draghi.[4] The general conclusions of Jürgensen are the same as those of Bauer. He states that the increase in nitrogen in the case of the well-nourished animals is absolutely greater after loss of blood than in fasting animals, but that it is smaller in comparison with the quantity of proteid available. Jürgensen's experiments are interesting but his failure to give his data for the control experiments upon dogs in a condition of nitrogen equilibrium is to be regretted.

Fraenkel[5] takes exception to the conclusions of Bauer and Jürgensen, and claims that the increased proteid decomposition follows the diminished oxygen supply, due to the lowering of the oxygen carrying power of the blood. This theory is not approved by v. Noorden,[6] Jürgensen and others.

Ascoli and Draghi, in observations upon human subjects and upon dogs, came to the conclusion that there was no increased nitrogen elimination following the loss of blood. The non-occurrence of a rise in nitrogen after hemorrhage is based on the theory that the organism contains a certain reserve supply of blood which may be removed without detriment to the body (the "luxus blood" of Maragliano).

Observations upon the variation in the respiratory exchange, after hemorrhage, have been made by Bauer, Lukjanow,[7] and Gürber.[8] Experiments by Bauer in a respiration apparatus of the Voit model, using fasting dogs as subjects, showed the excretion of CO_2 to be practically unchanged in the 12 hours following

hemorrhage, while the oxygen absorption decreased about 15%. Forty-eight hours later the amounts of both CO^2 excreted and O absorbed had decreased greatly. In well-nourished dogs there was an increase of 4% in CO_2 excreted during the first 12 hours after hemorrhage and an increase of 22% in the oxygen absorbed. After 24 hours the values for both CO_2 and O sank appreciably. Bauer concluded that the decrease in CO_2 excretion after hemorrhage showed that the destruction of fat had decreased and pointed to the storing of fat in anaemic and chlorotic patients as verification.

Gürber, as a result of observations on well-nourished rabbits, drew the conclusion that the respiratory exchange was effected very little if any after hemorrhage, and that the variation when observed was in the form of an increase. Lukjanow investigated the effect of oxygen inhalation after hemorrhage. Two experiments were made on rats and one on a dog. In every case one hour after the hemorrhage the absorption of oxygen was increased.

Among the numerous observations upon the alteration in the number of red corpuscles or the percentage of haemoglobin following hemorrhage those of Autokonenko,[9] Baumann,[10] Luzet,[11] Vulpain,[12] Hünerfauth,[13] Buntzen[14] and v. Lesser[15] are of particular interest. All of the experiments of Autokonenko were made on dogs. His animals were always fed a constant diet between 9 and 10 A. M. and the operations occurred between 3 and 4 P. M. The author concluded that the number of leucocytes began to increase from the first hour after blood-letting, the maximum being reached at the end of the first day. The increase was principally in small leucocytes. If a second hemorrhage was induced when the leucocytes were still greatly increased a leucocytosis more prominent than the first, but of less duration, occurred. A third hemorrhage produced no further increase. Baumann in a series of very complete experiments on dogs observed a general deterioration in the blood and serum following hemorrhage, especially in the former. The quantity of haemoglobin he found to be reduced 21%, the number of red corpuscles 14%, and the specific gravity 1%. The solids, proteids and total nitrogen of the blood and serum underwent a decrease of about 12% each. The

leucocytes were increased about 40%. Serum albumin was found to have been greatly increased at the expense of the serum globulin. Fibrin was increased and the coagulation rate shortened while the ash remained unchanged.

Luzet, as the result of investigations on pigeons, found a decrease in red corpuscles and haemoglobin and an accompanying leucocytosis. The work is of interest in indicating the similarity of post-hemorrhagic effects in man, lower animals and birds. The conclusions of Buntzen from experiments on dogs are interesting:—1. Red corpuscles decreased 5% in 10 minutes. 2. Diameter of red corpuscles decreased. 3. No increase in leucocytes. 4. Volume of blood restored in a few hours after a hemorrhage of 1-2% body weight. Loss of over 4% took over 24 hrs. to restore. 5. Red corpuscles normal, after hemorrhage of 1.1% to 4.4% of body weight, in 7 to 34 days. 6. Percentage of solids in the serum decreased from 11.5% to 10.1% in successive drawings.

The failure of the author to observe any increase in leucocytes after hemorrhage is contradictory to nearly every authentic observation.

Hünerfauth investigated the influence of "traumatic anaemia" in frogs, rabbits and dogs. The observations on frogs show that in an hour after a hemorrhage of less than 2% body weight a very noticeable decrease in the number of red cells was seen, and a lesser decrease in amount of haemoglobin. A strong leucocytosis also existed. Regeneration was shown to be slow in the frog. Regeneration in the frog was also studied by Vulpain, who found it to be much slower than in man and the lower animals. Six weeks after the hemorrhage the cells in the marrow destined to form new red corpuscles were small and totally colorless.

Investigations of more or less value have been carried out by Lyon,[16] Bizzozero and Salvioli,[17] Monassein,[18] Tschudnowsky,[19] Rieder,[20] and Hayem.[21] Bizzozero and Salvioli claim that a hemorrhage of 1% body weight produced a decrease of 11.14% in the haemoglobin and that this ratio holds generally. In a series of observations on a large number of different subjects (leech, mouse, mole, rabbit, hare, hen and pigeon) Monassein found the

red corpuscles to increase in size after hemorrhage. He explained this as being due to an imbibition of the diluted plasma.

Investigations made upon animals, in which the change in the number of leucocytes following hemorrhage was observed, have been promoted by Hayem, Rieder, Himmeljsterna,[22] Tschoudnowsky, Virchow,[23] Limbeck,[24] and Molassez.[25] Hayem observed a leucocytosis which he ascribes as arising rather from the inflammatory process than from the loss of blood. Limbeck observed a similar leucocytosis, and also found an increase in leucocytes following simple incision, when no blood was drawn and the wound healed with no suppuration. Tschoudnowsky found such a rapid leucocytosis that the ratio of leutocytes to red corpuscles was as high as 1:60. Virchow explained post-hemorrhagic leucocytosis as being caused by the property the leucocytes have of clinging to the walls of the vessels when the other constituents are drawn off. In a series of experiments on dogs Rieder observed a variable leucocytosis after hemorrhage. In one case the number of leucocytes was double the normal on the third day, while in another case it was very feeble at that period. Himmeljsterna reported the unique observation of a decrease in leucocytes on the first day after hemorrhage.

Henle,[26] Remak,[27] Woltersom,[28] Conheim,[29] Massart and Bordet,[30] Gabritschewsky,[31] Afanasiew,[32] Leber,[33] Roemer,[34] Buchner,[35] Escherich,[36] and Foster [37] all report the observation of a leucocytosis of greater or lesser intensity following hemorrhage. Afanasiew reports an increase in the leucocytes amounting to 15 times the normal.

The influence of the loss of blood upon the nervous system has been investigated by Leichtenstern,[38] Kussmaul and Tenner,[39] Naunyn and Quinke,[40] and Gies.[41] Leichtenstern observed that immediately after hemorrhage a temporary decrease in the number and depth of the respirations took place. After severe hemorrhages the frequency of respiration ultimately increased. Kussmaul and Tenner observed convulsions due to a decrease in the aterial blood supply of the brain. These convulsions did not occur in slow hemorrhages. The authors showed the central origin of the convuslions to be in the region behind the optic lobes. This

investigation of Kussmaul and Tenner, as well as others by Jolly and Donders, has shown that the statement that the loss of blood does not alter the blood supply to the brain is without foundation. In experiments on toads, frogs, rabbits and dogs Gies induced anaemia of the brain by means of perfusing solutions. He observed that rapidly induced anaemia was followed by convulsions, whereas an anaemia brought about gradually was unaccompanied by any such phenomena.

Experiments upon the variations in blood pressure after hemorrhage have been made by Worm-Muller,[42] Volkmann,[43] Nawrotzky,[44] Magendie,[45] Nawlichen[46] and Hayem,[47] while observations upon the variations in body temperature after hemorrhage have been made by Marshall Hall,[48] Traube,[49] Spielman,[50] Frese and Charaszewski,[51] and Wunderlich.[52]

The fibrin content of the blood has been made the subject of investigations by Bücke,[53] Nasse,[54] Jürgensen,[55] and Mayer.[56] Brücke found a decrease in fibrin proportional to the amount of depletion. His observations were made upon several samples, drawn consecutively. He attributed the decrease in fibrin to the fact that transuding fluids had diluted the blood. Nasse, by drawing the blood at intervals of 48 hours, showed an increase in fibrin, and Jürgensen by similar procedure on fasting dogs, confirmed this observation. Baumann and Mayer found the same.

The rate of coagulation has been studied by Vierordt,[57] Brücke,[58] Nasse,[59] and Baumann.[60] Vierordt and Brücke reached the conclusion that in uninterrupted hemorrhages the coagulation rate gradually shortened. Nasse, by drawing his samples at intervals of 24 hours, found the coagulation rate to lengthen. Baumann after an interval of a week found the coagulation rate shortened. Probably much depends upon the individual organism and the amount of blood drawn.

Observations upon the specific gravity of the blood have been made by Sherrington and Copeman,[61] Otto,[62] Jones,[63] Bizzozero and Salvioli,[64] Woltersom,[65] and Baumann.[66] In every case the specific gravity was observed to fall after loss of blood.

Variations in body weight after hemorrhage have been noted by Tolmatscheff,[67] Bauer,[68] Jürgensen,[69] Lister,[70] and Hünerfauth.[71] An increase was generally observed. Tolmatscheff in-

duced six hemorrhages upon one dog in a period of 70 days and observed an increase in body weight up to the fifth hemorrhage, when a decrease occurred. His hemorrhages were from 1.1% to 2.8% of the body weight. In experiments already quoted upon nitrogen metabolism Bauer and Jürgensen observed a slight rise in body weight. Lister mentions the fattening of calves in England through frequent blood-letting. Hünerfauth observed in dogs an increase in weight during the week after hemorrhage.

The rate of the urine flow after hemorrhage has been investigated by Frederick Goll.[72] Dogs narcotized by opium were used as subjects. Ureter cannulas were inserted and the normal flow of urine was observed for one-half hour when a hemorrhage was induced and the variations in the flow of urine and in blood pressure were recorded. In every case the urine flow was greatly decreased after hemorrhage, and this decrease was accompanied by a fall in blood pressure. The author concluded from his observations that arterial pressure had an important influence upon the excretion of urine. Jürgensen observed an increased urine flow after hemorrhage, especially in the case of fasting dogs. He offered two suggestions for the increased volume:—1. Extra water needed to remove the accumulated urea. 2. Tissue fluids contain less proteid and more water than the blood. By transudation after hemorrhage the blood would contain more water than normal if it were not removed in the urine.

"Fatal hemorrhage" has been the topic of investigations by Schramm,[73] v. Kireeff,[74] Hayem,[75] and Noll.[76] Schramm placed the limit as varying between 3.91%—5.77% of the body weight, while Hayem placed the value at from 4.34%—5.55% depending on the individual. v. Kireeff ascertained that a loss of between 56% and 95% of the total blood was necessary to cause death, whereas Noll found that a hemorrhage of ⅔ the total blood was fatal.

Infusion experiments of various forms have been promoted by Kronecker,[77] Ott,[78] Maydl,[79] Schramm,[80] and Prevost and Dumas.[81]

The influence of iron feeding upon blood regeneration following hemorrhage has been investigated by Skvortsov,[82] and Debierre and Linassier.[83] The results of both observations showed

an increase in haemglobin and red corpuscles after iron feeding was begun. An increase in lymph formation was obtained by Emminghaus[84] after hemorrhage.

Proteid decomposition in patients suffering from various maladies has been studied by Fleischer and Penzoldt,[85] Lipmann-Wulf,[86] Ketcher,[87] v. Moraczewski,[88] and Eichorst.[89] The observations of Fleischer and Penzoldt were concerned with conditions pertaining in Leukaemia patients. Normal persons were used as controls and were fed the same diet as the patients. The urine was analyzed for nitrogen, sulphur, phosphorus and uric acid. The data showed that all four of these constituents were increased in leukaemia. Lipmann-Wulf in three cases of chlorosis observed a gain of nitrogen to the body varying from 0.06 to 0.71 gram per day. However, the nitrogen content of the food was determined by calculation, and the feces was not analyzed. Eichorst, on the contrary, claims to have observed an increased proteid decomposition in pernicious anaemia. He simply makes his deductions from general indications as no food analyses were made.

The effect of the inhalation of oxygen in diseases where a pathalogical blood condition maintains has been investigated by Burzhinski,[90] Sticker,[91] Albrecht,[92] and Hayem.[93] The observations of Burzhinski show an increased nitrogen metabolism in leukaemia patients. Uric acid in relation to urea was also increased. Studies by Albrecht on anaemic children who inhaled thirty litres of oxygen daily showed increased respiration, pulse, body temperature and weight. The red corpuscles were increased in direct ratio to the amount of oxygen inhaled and the haemoglobin value was also raised.

Post-hemorrhagic observations of leucocytes have been made by Rieder,[94] Hayem,[95] Samuel,[96] and King.[97] Rieder observed that the leucocytosis following hemorrhage in man did not differ from other forms of leucocytosis. He found nucleated red corpuscles and a decrease in haemoglobin. Hayem failed to observe any post-hemorrhagic leucocytosis in human subjects. The red corpuscles and haemoglobin were decreased. Samuel observed that the number of the leucocytes was increased after hemorrhage, due to the large number which were brought by the lymph.

Post-operative leucocytosis was observed in several instances

by King. The operations were of various kinds of the major order. The maximum leucocytosis in the majority of cases occurred within twelve hours after the operation and was very transient. The author's observation of leucocytosis following operative procedure agrees with those of Molassez, and Hayem. These latter investigators however were inclined to believe the leucocytosis was due to suppuration or inflammation, whereas no such condition was present in King's experiments.

Mosler,[98] Lowit,[99] and Müller[100] have observed conditions in leukaemia. Lowit claimed that the large number of leucocytes in the blood in leukaemia was not due to increased production of leucocytes but to a lessening of the formation of polynuclear cells from the mononuclear, as well as to the diminution in the destruction of polynuclear cells. Müller believed the increase in leucocytes was due to increased cell proliferation.

The observations upon the influence of the loss of blood occurring pathalogically in human subjects are comparatively few in number. Such losses would ordinarily occur from accident, in rupture of aneurism, in post-partum hemorrhage, or in cases of ulcer of the stomach or duodenum. Osler[101] mentions an instance where 7½ pounds (3375 grams) of blood was shed into the pleura from the rupture of an aneurism. In a case of hematemesis the same authority mentions that a loss of 10 pounds (4500 grams) in one week was followed by recovery. The author states that even after very severe hemorrhages of this order, the number of red corpuscles is not reduced so greatly as in forms of idiopathic of pernicious anaemia. Thus in the above instance after a week of bleeding the red corpuscle count was as high as 1,390,000 per cubic millimetre. Regeneration goes on rapidly and sometimes the blood is normal as regards volume and content of salts and proteid constituents, in a week or ten days. This regeneration may, however, take weeks or even months, Osler says, before the corpuscles reach the normal standard. The haemoglobin is restored more slowly than the corpuscles, and there is a moderate leucocytosis which diminishes during recovery.

Nitrogen metabolism during gastric ulcer was studied by v. Noorden,[102] Neusser,[103] and Kalisch.[104] v. Noorden observed in two cases, where the loss of blood was large, that no considerable

increase was noted in the nitrogen elimination, either on the day of the loss of blood or on the following days. The patients took no food and the nitrogen output was from 6.2 to 8 grams per day, an amount which was about normal for the organisms during inanition. From this the author was inclined to doubt whether the increase in nitrogen observed by Bauer, Jürgensen and others would hold in the case of man.

B.—FIRST SERIES OF EXPERIMENTS.

I. DESCRIPTION.

1. **The Purpose and Plan of the Investigation.**—The purpose of this investigation was to study, in dogs, the effect of external hemorrhage upon the general metabolic processes of the body, particular attention being paid to the changes occurring in the volume of the urine and in the course of the nitrogen, sulphur and phosphorus output. It was also proposed to study the variation in the chemical composition of the blood following hemorrhage. Alterations in body weight were also recorded. It was determined to use one subject for a series of experiments and to study the influence of repeated hemorrhages extending through a long period of time, and later to check these results upon a second animal.

After the first dog was brought to a condition of nitrogen equilibrium by means of a preliminary experiment, the initial hemorrhage was instituted. Following this, after the dog was again at nitrogen equilibrium came the control experiments. These were followed by four more hemorrhages of varying intensities and separated from one another by periods of different lengths. The first, second, third and fourth hemorrhages were made with the animal practically in nitrogen equilibrium, whereas in the case of the fifth hemorrhage no attempt in this direction was made. We fully appreciate that at the time of this last hemorrhage the organism was somewhat abnormal and that therefore the results are

not strictly comparable with those of the earlier hemorrhages. However, as long as we were able to get the organism in a condition of nitrogen equilibrium we hold that no great abnormality could obtain, and that therefore we are justified in comparing the data from the first four hemorrhages.

General data for the first series of experiments are given in Table XII.

2. **Articles of Diet.** *Beef.*—This consisted of lean meat (round steak) carefully freed, as far as possible mechanically, from all traces of fat and connective tissue. After being finely hashed in a meat chopper the meat was thoroughly pressed in a hand press, carefully mixed and samples taken for analysis. This sampling was done by taking small portions from various parts of the mass during the mixing process and weighing by difference in tubes previously freed from moisture by means of filter paper. After being pressed and mixed the beef was made into small balls and placed in air-tight glass jars. These vessels contained, at most, only enough meat for two days' use, thus necessitating the opening of any single jar but once.

The meat was prepared in quantity sufficient to last several weeks, and for preservation was placed in the "cold room" where it was frozen, thus insuring uniform composition from day to day. Proof of this uniform composition after the lapse of time was shown by the duplication of analytic results three weeks after the beef had been placed in the jars. We feel that this method serves admirably for the purpose intended. The beef is at all times fresh and palatable and eagerly eaten by the animals under investigation. In any experiments where use is made of fresh meat and where freezing facilities are at the command of the investigator, we highly recommend this method of meat preservation and preparation.[1]

Cracker Dust.—Ordinary cracker dust purchased in quantity from a wholesale grocer, thoroughly mixed and placed in large air-tight anatomical jars.

Lard.—Pure leaf lard and containing nothing of a vegetable nature.

Bone Ash.—Obtained from a well known firm of wholesale

[1] Gies: American Journal of Physiology, 1901, V., p. 235.

chemists. The feces of dogs living upon a meat diet are ordinarily passed in large quantity at intervals of several days and being of a very soft character are extremely unpleasant to deal with. Feces of this order will invariably become distributed over a great portion of the interior of the cage and frequently mix with the urine, thus making impossible accurate deductions regarding the nitrogen content of either the one or the other. In order to cause more regular defecation of feces having a more desirable consistency it was determined to feed the animal ten grams of bone ash daily. With this amount of ash in the diet the animal defecated eighty times in eighty-four days or approximately once a day, and with two exceptions the stools were invariably of a hard character and easily removable.

Water.—Ordinary city water heated to about fifty degrees centigrade. The water was taken at this high temperature in order to offset the low temperature of the frozen beef and at the same time form a tempting mixture. When added to the solid ingredients of the diet this warm water formed a rather thick soup which was decidedly appetizing. The food mixture as finally prepared possessed a temperature of approximately twenty-three degrees centigrade and was always eaten by the dog with great eagerness.

By referring to Table I, the quantity of each of the articles of diet fed during the various periods may be observed. This diet containing 10.271 grams of nitrogen, was given the beast at 5 o'clock every afternoon. It was of course very desirable, from the nature of the investigation, that the subject should ingest the same amount of nitrogen daily the entire experimental period. Therefore, when the original preparation of beef was consumed, enough of the new preparation was fed to give the same amount of nitrogen daily. Thus the different beef preparations were fed as follows:—

Preparation No. 1.—250 grams daily from Nov. 2 to Dec. 4.
Preparation No. 2.—256.4 grams daily from Dec. 5 to Jan. 2.
Preparation No. 3.—241 grams daily from Jan. 3 to Jan. 24.

Apart from the beef the amounts of the constituents of the diet fed daily were unaltered during the entire experimental period of eighty-four days.

3. **Preparation of the Anaesthetic.**—The ether used in all operations was the purest product obtainable on the market. This presumably chemically pure ether was dehydrated by fused copper sulphate for several days, and after being subjected to a series of three distillations the final product was that used as the anaesthetic in our operations.

The chloroform was also the best obtainable and was used as purchased.

4. **Subject.**—In all long metabolism experiments upon dogs where so much of the success of the investigation depends upon the subject it is evidently of great importance to secure a dog that will eat his food regularly, be contented in confinement, and possess an amiable disposition. Where the income and outgo of nitrogen are studied it is also desirable to use a short-haired dog, as in the course of a long experiment much nitrogen is lost by way of the hair. In the present instance three beasts were tried before a suitable subject was found. The third animal, however, a very active short-haired dog weighing about 17k. was entierly satisfactory.

5. **Methods of Analysis.**—The nitrogen determinations were made by the Kjeldahl method, the preliminary oxidation being accomplished by sulphuric acid and a small amount of copper sulphate.[1] The chlorine content of the urine was determined by Mohr's[2] method. Sulphur and phosphorus were determined by the fusion method.[3] The specific gravity of the blood and urine was determined by an urinometer.

The analyses in every instance were made in duplicate.

The analytic results were further controlled by the preparation and analysis of composite urine samples for each experimental period. In Table XIV are given the data from the analyses of these urines.

Nothing except the purest chemicals available were employed and these were always examined and "checked" before use.

[1] Marcuse: Archiv für die gesammte Physiologie, 1896, LXIV., p. 232.

[2] Neubauer and Vogel: Harnanalyse (Modification of Neubauer and Salkowski), 1898, p. 709.

[3] Hawk: University of Pennsylvania Medical Bulletin, 1905, XVIII., p. 7.

II. PRELIMINARY EXPERIMENT.

In all investigations where a nitrogen balance is attempted it is of the first importance to bring the organism to be used as subject to the point of nitrogen equilibrium before any accurate study of the specific problem shall be attempted. To this end, the dog mentioned on page 19 was selected as a subject and preliminary feeding of the animal begun on Oct. 29, 1902. During the first few days no analyses of excreta were made but the animal was given the regulation diet. In the course of this period his body weight fell from 17.23k. on Oct. 29 to 17.02k. on Nov. 1. Beginning Nov. 2 full analytical data were collected.

This preliminary experiment embraced a period of twelve days. In that time, upon a regular daily ingestion of 500 cc. of water the dog excreted an average daily volume of 489 cc. of urine. Making allowance for the evaporation which must of necessity have been several cubic centimetres daily we see that practically all of the ingested water was recovered. It will be noted that the body weight of the animal was wonderfully regular during the early days of the experiment and even at the twelfth day showed but a slight decrease.

For this preliminary period the average nitrogen output was 9.673 grams daily (Table III). The reaction of the urine was acid throughout the period. For the purpose of direct comparison with other data the last five days of the experimental period are alone taken into account. Naturally the first days of the experiment when the dog was among totally new surroundings and being fed an unaccustomed diet, the collected data would have comparatively little value. However, as he became accustomed to both diet and conditions the organism would gradually assume a definite nutritional plane and nitrogen equilibrium would result. Our data make it evident that from the eighth to the twelfth day, inclusive, the animal was rapidly approaching this condition. During these five days the average daily volume of urine was 517 cc. It will be noted that the average urine volume for the first seven days was but 468 cc., indicating an evident retention of water by the organism. Therefore the increase in volume during the following five days was to have been expected. During this same five day period, upon a daily nitrogen ingestion of 10.271 grams,

10.023 grams was eliminated, thus showing a gain of but 0.248 gram daily (Table IV). This then afforded a very satisfactory starting point for our study of the influence of hemorrhage.

III. FIRST HEMORRHAGE

In determining the influence of the withdrawal of blood upon metabolism it is in many ways desirable to take the fluid from a small vessel supplying a comparatively unimportant area. At first thought the facial vessels seem to offer many advantages in this direction. The ligation of these vessels, taking their course as they do along boney structures, would naturally occasion less disturbance of the metabolic activities than the ligation of vessels of the same calibre in many other parts of the body. It was ascertained, however, by means of a preliminary examination of these vessels in another animal, that it would not be expedient to attempt to draw any large amount of blood from this locality. Therefore, after due consideration, it was determined to make use of the femoral artery somewhere along the lower portion of its course (Saphenous branch).

1. **Operative Procedure.**—The subject of this experiment was a 17k. dog which had been on a fixed diet (See page 55) since Oct. 29 and was now, after sixteen days feeding, approximately in nitrogen equilibrium (See Table IV, p. 58).

In order to make impossible the loss of urine should any be voided during anaesthesia, the beast was placed in a large zinc-lined tray. Urine passed under these conditions could easily be recovered by means of a pipette and filter paper. At 8.10 A. M. the administration of the anaesthetic was begun. From the very first the beast struggled in a very violent manner, necessitating the combined efforts of three men in order to administer the anaesthetic at all satisfactorily. At the end of eight minutes, as the animal still possessed much of his original vigor, a small amount of chloroform (5 cc.) was added to the ether previously administered. This chloroform-ether mixture had the desired effect and the dog was soon in a semi-unconscious condition. Ether was now continued and at 8.45 it was plainly evident that it had been administered to the surgical degree. The operation

was begun at this time, and precautions were taken throughout to keep the conditions strictly asceptic.

Before laying bare and clamping the artery the following arrangements were made: A cannula previously coated on the interior with an extremely thin layer of mutton tallow, to prevent the blood from clotting, was adjustetd to a rubber tube of appropriate length and calibre. In collecting the blood use was made of a 25% solution of sodium chloride, as it was desirable to prevent clotting as far as possible. A large beaker containing 273 grams of the sodium chloride solution (244 cc.) was accurately weighed, after which both balance and beaker were carefully supported in a position very near and somewhat below the operating table. The balance was placed in this position in order to make the length of tube leading from the cannula to the beaker as short as possible and in this way further guard against clotting. It had previously been determined to withdraw an amount of blood approximating 3% of the animal's body weight, or about 500 grams. To accomplish this accurately a 500 gram weight was added to the weights of the beaker and salt solution and it was then arranged to allow the hemorrhage to continue until it was evident from the movement of the balance pan that approximately the desired amount had been collected. As soon as possible after the completion of the above arrangements the artery was laid bare and the blood drawn.

In forty-six minutes from the time the anaesthetic was discontinued the dog was entirely himself, stood on his feet, and although he was somewhat weak from loss of blood and the effect of the anaesthesia, he appeared in fine condition. At no time after the operation was there any inclination to vomit, and the appetite of the animal continued excellent throughout the period.

Time Schedule.—8.10 A. M., anaesthesia begun (ether). 8.18, trace of chloroform given. 8.35, beast placed on board. 8.45, operation begun. 9.26, incisions made, artery laid bare, and ligated, cannula inserted and slow hemorrhage commenced. 10.00, commencement of more rapid hemorrhage. 10.12, return to slow hemorrhage. 10.14, hemorrhage ended. 10.20, wounds sewed up and administration of ether discontinued. 10.21, beast removed from board to cage. 10.25, evidence of returning con-

sciousness. 10.55, sat up in his cage. 11.06, stood on his feet and moved about. The blood drawn at this hemorrhage weighed 492.9 grams (Table II).

2. Observations on the Influence of the First Hemorrhage.—The first observation following the hemorrhage was the failure of the dog to urinate as frequently or as large a volume as formerly. The experiment started at 8.10 A. M. and the first urine was not passed until from 16 to 24 hours afterward (Table V). The urine volume for the day of the operation was therefore the lowest of any day of the investigation up to that time. Now in our control experiments we have seen that under the influence of the anaesthesia, in each case, the first urine was passed in from 7 to 8 hours after the operation. It is also seen from our data that on the first day of the control experiments the maximum volume of urine was eliminated. Therefore this very low volume after hemorrhage is all the more significant when we consider that the same force (anaesthesia) was acting at the time of the hemorrhage as was at work when we secured the very large urine elimination on the initial days of our control experiments. The only new factor is the hemorrhage. Hence the influence of the withdrawal of blood is much greater than appears, for in order to so delay the flow of urine that the first elimination should not occur until from 16 to 24 hours after, the hemorrhage has been forced to overcome the diuretic influence of the anaesthesia which would have caused a large output of urine in from 7 to 8 hours after.

The nitrogen content (6.33 grams) of the urine on the first day, was also the minimum output up to date. The body weight of the dog fell 0.51k. on the first day. On the second day some radical changes occurred. On this day the dog passed an unusually large volume of urine, having the maximum specific gravity for the experiment, and containing the second largest content of nitrogen. The body weight of the dog continued to fall somewhat.

Notwithstanding the rather high volumes of urine passed on the second and third days after the hemorrhage, the average at any time was considerably below that of the preliminary experiment. For instance, the average of the first nine days was but 467 cc., whereas the average preceding the hemorrhage was 489 cc. This

showed an average retention by the organism of 22 grams of water daily, or 198 grams in the nine days. During the last seven days of the experiment the retained water seemed to have been eliminated and the normal ratio again reached. In the course of these seven days the average urine volume was 518 cc., a daily increase of 29 cc. above that of the preliminary experiment, or a total increase of 203 grams. From the weights as determined we find that during this period of seven days the dog's weight fell from 16.34k. to 16.09k., a total loss of 250 grams.

3. **Discussion of the Income and Outgo of Nitrogen, Sulphur and Phosphorus After the First Hemorrhage.**—The study of the first hemorrhage was begun with the subject showing a gain of 0.248 gram of nitrogen daily. The effect of the withdrawal of blood was to cause an increase in the nitrogen content of the urine, this increase appearing the first day after the hemorrhage, and reaching its maximum at the fifth day. After this date the average elimination decreased and approximate nitrogen equilibrium was reached on the sixteenth day of the experiment.

By referring to the data for the nitrogen elimination for the five days following this hemorrhage (Table IV), it will be seen that the average daily increase in nitrogen for this period was 1.009 grams. The dog was gaining 0.248 gram of nitrogen daily, however, at the time of the hemorrhage, hence the effect was to cause an increased output of 1.257 grams of nitrogen daily. This represents the final effect produced by the anaesthesia, operation and hemorrhage acting in unison. Now we shall see from our control experiments (Table XIX), that the effect of the anaesthesia was to decrease the nitrogen output 0.937 gram daily. Making this correction we have as the effect of operation and hemorrhage an increase of 2.194 grams daily, and further correcting for the effect of the operation we have as the net effect of the hemorrhage an increase in the daily nitrogen output of 0.488 gram (Table XIX).

The nitrogen balance for the whole sixteen days of the experiment (Tabie III) showed a loss of 0.179 gram of nitrogen daily. The sulphur followed this with a daily loss of 0.023 gram (Tables VI and XI) while the phosphorus showed a daily gain of 0.123 grams.

IV. CONTROL EXPERIMENTS.

In studying the effect of the withdrawal of blood there were evidently two forms of control experiments necessary before any definite conclusions could be reached. The first of these was the influence of anaesthesia, and the second the influence of the anaesthesia plus the influence of the operation which accompanied all our withdrawals of blood. If it were practicable to draw blood without the use of any anaesthetic, obviously the first form of control experiment could be eliminated. But even were such a method pursued other factors, such as the nervous influence, would be introduced and we could not be certain that the effect secured was dependent alone upon loss of blood. Obviously, for this reason experiments upon the influence of hemorrhage, made without the use of anaesthetics, would be extremely difficult to control. Local anaesthetics might be employed, but even here we could not be sure what influence the absorption of these bodies would have upon the organism. The experimental plan adopted by us was open to complete control which we feel would not have been possible had we followed either of the other plans mentioned.

Two control experiments were made, the first, ten days in length, was devoted to the study of the influence of anaesthesia, and in the second, covering a period of thirteen days, an attempt was made to determine the effect of anaesthesia accompanied by the operative manipulation.

1. **Influence of Anaesthesia.**—The general procedure in this our first control experiment was practically identical with that of the regular blood-letting experiments. The animal was placed on the operating board, loosely tied to allow freedom of motion in his struggles, and the administration of ether begun. After an interval of a few moments a small amount of chloroform was given as in the other experiments. Care was taken to consume the usual length of time in reaching complete anaesthesia. The beast was kept under the influence of the anaesthetic for a period corresponding to the normal time of operation and was then returned to his cage. A detailed time schedule follows:—9.10, anaesthesia begun. 9.18, chloroform administered. 9.40, anaesthesia com-

plete. 11.20, administration of ether discontinued and dog returned to cage. 11.30, returning consciousness. 11.50, sits up and staggers about. 12.00, appears normal. The whole period of anaesthesia was without incident except the loss of about 5 cc. of urine at 9.15 by reason of vigorous abdominal movement. This urine was recovered by means of filter paper and added to the washings for the period. The struggling incident to the former anaesthesia was duplicated in detail.

(a). **Observations on the Influence of Anaesthesia.**

Before attempting to study the influence of anaesthesia an effort was made to get the dog as nearly as possible in a condition of nitrogen equilibrium. By referring to the nitrogen balance for the five days immediately preceding the anaesthesia experiment (Table IV, p. 58) it will be seen that the animal was approximately in the desired condition, there being a loss of but 0.159 gram of nitrogen per day.

Upon an examination of the data for this experiment (Table XII, p. 66) several evident variations from the order obtaining in the preliminary and first blood-letting experiments are noted. Whereas the average urine volume of the preceeding periods had been 489 cc. in each case, here, upon the same ingestion of water we secured an average urine volume of 522 cc. for the period. The urine volume for the day on which the anaesthetic was administered was particularly worthy of notice. Upon this day, which in the experiment preceeding had shown a urine volume of 377 cc. we secured a volume of 654 cc., or nearly double that previously secured. When we compare this volume with the average volume for the whole period preceeding we still have an increase of 165 cc. for the day. This increase in volume is evidently traceable to the diuretic action of the ether.

Another striking feature of the urine excretion was its high specific gravity accompanied by a relatively low nitrogen content. This was especially true of the first few days following anaesthesia. As measured by other daily excretions, both before and after the anaesthesia experiment, a urine volume of 654 cc. having a specific gravity of 1.018 would have given us a nitrogen output of 10.94 grams (See data for Nov. 10, Nov. 24, Jan. 12, and

Jan. 13). Thus the effect of the anaesthesia was to diminish the total nitrogen excretion for the day approximately 20%.

After the excretion of phosphates and sulphates failed to show the cause of the unusual relation between the specific gravity and nitrogen content we turned to the chlorides for a solution of the problem, and beginning Nov. 25 duplicate determinations of the chlorine content of the urine were made for every day up to and including Dec. 3. The following results were obtained:—

Nov. 25———1.82 grams of chlorine.
Nov. 26———1.71 grams of chlorine.
Nov. 27———1.65 grams of chlorine.
Nov. 28———1.87 grams of chlorine.
Nov. 29———1.69 grams of chlorine.
Nov. 30———4.37 grams of chlorine.
Dec. 1———2.85 grams of chlorine.
Dec. 2———2.73 grams of chlorine.
Dec. 3———2.39 grams of chlorine.

From this data it will be seen that the chlorine output was fairly constant up to the day the anaesthetic was given, showing an average daily elimination of 1.75 grams, and that on this day an increase of 150% in the chlorine content of the urine occurred. Thus the indications are that the rise in the daily output of chlorides through the influence of anaesthesia, caused a higher specific gravity on the days immediately following the administration of the anaesthetic than the determined content of nitrogen would warrant.

As a further verification we took a volume of water (649 cc.) equal to the volume of urine passed by the dog on Nov. 30, and dissolved in this 7.2 grams of sodium chloride, which, according to our data, was the amount eliminated on that day. This gave us a specific gravity of 1.009. The actual specific gravity of the urine of that day being 1.018, we see that a large part of the density of the fluid was due to the presence of sodium chloride. We next added to this sodium chloride solution an amount of urea (18.4 grams) equivalent to the nitrogen content of the urine for that day, and secured a specific gravity of 1.015. This left but three points in density to be met by the other solid ingredients of

the urine. Thus we secured from 7.2 grams of sodium chloride a rise in specific gravity 50% greater than from 18.4 grams of urea. This rough calculation easily explained the condition of high specific gravity and low nitrogen content.

As has been said elsewhere (p. 23) the drawing of blood, among other well marked effects, caused a very noticeable decrease in the amount of urine eliminated for an extended period thereafter. Consider, for example, the hemorrhages immediately preceeding and following the anaesthesia experiment. After the first hemorrhage which began at 8.10 A. M. no urine was passed during the next sixteen hours, or up to midnight (Table V). On the following morning at 8.30 the urine volume was 300 cc. As the beast was not observed between midnight and 8.30 A. M. we are unable to conclude at what hour this urine was eliminated. After the second hemorrhage a similar course was followed, *i. e.,* no urine up to midnight, followed by a volume of 590 cc. at 9 o'clock the next morning. In the anaesthesia experiment, however, where no blood was drawn, but the individual influence of the anaesthetic was studied, we find very different conditions to prevail. Here, following the administration of the ether at 9.10 A. M., we observed a fairly large elimination of urine (283 cc.) in seven hours (4.15 P. M.) or in less than one-half the time that elapsed before the first urine appeared after the hemorrhages mentioned. The diuretic influence of the ether was thus very clearly indicated.

As was observed in the other periods, the body weight of the animal fell somewhat upon the day of anaesthesia, in this particular casea loss of 0.28k. being noted.

(b). Discussion of the Income and Outgo of Nitrogen, Sulphur and Phosphorus Before and After Anaesthesia.

It is very evident that an effect produced by an agency such as anaesthesia or hemorrhage will naturally be more pronounced during the days immediately following the operation. It is also easily seen that in all such instances there will come a point, sooner or later, at which time the animal will again begin to approach the normal and tend toward nitrogen equilibrium. Such being the situation it is of course essential to know as nearly as possible

when nitrogen equilibrium is being reached. In order to facilitate comparison and the drawing of conclusions, nitrogen balances for a short period immediately preceeding the commencement of each experiment have been made in order to show the exact state of the organism at the moment the experiment began. In addition, nitrogen balances for a few days following the commencement of each experiment are given in order to show the immediate effect, if any, which was secured in each specific instance. No attempt being made after Jan. 19 to get the dog again into nitrogen equilibrium, such balances will not be found for experimental days after that date. As sulphur and phosphorus were not determined in daily samples no such balances will be found for these elements.

By referring to the nitrogen balance for the short period immediately preceeding the administration of the anaesthetic (Table IV) it will be seen that the dog was approximately in nitrogen equilibrium, and by consulting this table further we note that the effect of anaesthesia was to cause a lowering of the nitrogen output and a consequent daily gain of 0.937 gram of nitrogen to the body. Data concerning the relation between the nitrogen content and the specific gravity of the urine during this period will be found on page 26.

The course of the sulphur excretion in a general way followed that of the nitrogen. The period preceeding the anaesthesia experiment showed a daily loss of 0.023 gram of sulphur (Table VI), whereas the balance for the period showing the influence of the anaesthetic exhibited a gain of 0.015 gram of sulphur daily. Thus we had as the final effect of the anaesthesia upon the course of the sulphur excretion a daily gain of 0.128 gram.

The course of the phosphorus excretion seemed to be directly opposite that of nitrogen and sulphur. Showing before the experiment a gain of 0.123 gram of phosphorus daily (Table VII), we secured after the anaesthesia a gain of but 0.015 gram daily. In this instance the phosphorus showed a loss of 0.108 gram daily, whereas the nitrogen and sulphur each showed a gain. Thus the anaesthsia caused a fall in the daily excretion of nitrogen and sulphur and a coincident rise in the phosphorus excretion.

2. **Influence of Anaesthesia-Operation.**—The nitrogen content

of the urines of Dec. 6-9 indicating that the dog was approximately in nitrogen equilibrium (+ 0.158 gram of nitrogen per day) it was determined to begin our second control experiment on Dec. 10. Apart from the drawing of blood, the procedure in this experiment followed the same course as that of the regulation blood-letting experiments. The beast was anaesthetized and the customary operative steps were carefully followed. The regulation incision was made, artery laid bare, (in this case the right femoral) clamped and the cannula inserted. The wound was then sewed up and the animal returned to his cage. In fact everything was done to make this operation coincide in every detail with the regulation blood-letting operations. Schedule follows:—8.12 A. M. anaesthesia begun.[1] 8.20, small amount of chloroform given. 8.45, operation begun. 10.23, anaesthetic discontinued. 10.24, dog placed in cage. 10.28, signs of returning consciousness. 10. 40, sits up.

(a). **Observations on the Influence of Anaesthesia-Operation.**

In the main the characteristics of this period were similar to those observed during the anaesthesia experiment. Here with the same uniform water ingestion of 500 cc. we secured an average daily urine volume of 531 cc., thus comparing favorably with the average (522 cc.) of the anaesthesia period, but being in marked contrast to the average elimination (489 cc.) secured during our preliminary experiment.

The same condition of low nitrogen elimination, when approached from the point of view of specific gravity, maintained here as was seen to prevail during the early part of the anaesthesia experiment. Here as in the former instance we considered that a largely increased output of chlorine caused the peculiar relation.

In this experiment, as well as in the one devoted exclusively to the study of the influence of ether, we noted a copious flow of urine appearing much earlier than after the blood-letting operations. As in the anaesthesia experiment, this copious flow of urine was doubtless due to diuresis produced by the anaesthetic.

On Dec. 18 at about 1 P. M. the dog was observed lapping its

[1] The animal passed a few grams of feces during preliminary anaesthesia. This was added to the feces for the day.

wound, and upon examination it was found that a slight hemorrhage had been produced by the animal, probably by means of his foot in the act of scratching. The flow of blood was soon stopped, however, and the wound bandaged with adhesive plaster to prevent the animal producing another hemorrhage. Probably not over 25 cc. of blood was lost and practically all of this was eaten by the dog. By an examination of the data it will be seen that the nitrogen elimination of Dec. 18 was the highest of the experiment, while that of Dec. 19 was also relatively high. This increase may have been due partly to the ingested blood, or it may have been the normal excretion since these two days were followed by two days of low elimination which upon the 21st practically restored the ratio as it existed previous to the accidental hemorrhage.

(b). **Discussion of the Income and Outgo of Nitrogen, Sulphur and Phosphorus Before and After Anaesthesia-Operation.**

The nitrogen balance for the four days immediately preceeding the commencement of the anaesthesia-operation experiment (Table IV) showed us that the dog was practically in a condition of nitrogen equilibrium (+ 0.158 gram daily). The next balance, *i. e.*, that for the five days immediately following the anaesthesia-operation of Dec. 10, records an average daily loss of 0.611 gram of nitrogen. Hence the effect of the anaesthesia-operation was to cause an increase of 0.769 gram in the daily nitrogen output (Table XIX). Now we have already seen that the effect of the anaesthesia alone was to decrease the nitrogen elimination 0.937 gram daily. Therefore the operation alone caused an increase in the nitrogen output large enough to overcome entirely the decrease due to the anaesthesia and yet show a daily increase of 0.769 gram. Hence the total increase due to the operation was 1.706 grams daily (Table XIX).

As was noted in the anaesthesia experiment the course of the sulphur excretion was very similar to that of the nitrogen. In the case of the phosphorus excretion also a uniformity with the conditions obtaining in the anaesthesia experiment was noted. Thus while the nitrogen and sulphur showed an increased daily elimination as a result of anaesthesia-operation the phosphorus excretion showed a decrease.

V. SECOND HEMORRHAGE.

This hemorrhage occurred on Dec. 23 at the close of the anaesthesia-operation experiment. An attempt was again made to withdraw approximately 3% of the animal's body weight. Apart from minor details the operative procedure was the same as that observed at the first hemorrhage (See p. 21). Two incisions were made as at the first operation. It was attempted to draw the blood from a branch of the left femoral just above the knee, but the vessel being too small at this point a second incision was made higher up and the main trunk of the femoral laid bare. A detailed schedule follows:—8.14 A. M., anaesthesia begun. 8.20, trace of chloroform. 8.40, first incision made. 9.12, second incision made. 9.30, cannula inserted. 9.31, hemorrhage begun. 9.40, hemorrhage ended. 10.05, anaesthetic discontinued. 10.10, wounds sewed up. 10.12, animal in cage. 10.24, returning consciousness. 11.40, dog appears normal.

The total amount of blood lost to the organism at this hemorrhage was 506 grams.

1. **Observations on the Influence of the Second Hemorrhage.**— According to Hammarsten[1] a hemorrhage amounting to one-fourth of the total blood produces no continued sinking of the blood pressure in the arteries; a loss of one-third reduces the blood pressure considerably and a loss of one-half, in adults, is dangerous to life. Now in our second hemorrhage on Dec. 23 we drew 506 grams of blood from the animal weighing at that time 15.72k. Taking the amount of blood present as being $^1/_{13 \cdot 5}$ of his body weight (Hammarsten's figure) or 1164 grams, it is seen that, according to Hammarsten, a hemorrhage of 582 cc. would be dangerous to life. The hemorrhage we produced amounted to 506 cc., and, as our data shows, the dog appeared as usual two hours afterward. It seems hardly probable that the animal's condition would have been materially different had we drawn 76 cc. more blood, thus securing ½ of his entire supply.

In the main the influence of the second hemorrhage seemed to be closely parallel to that of the first hemorrhage. At this second hemorrhage we noted the low volume of urine (428 cc.) on the

[1] Physiological Chemistry, Fourth Edition (English), 1904, p. 209.

day blood was drawn, followed by a period of 16-25 hours (Table V) during which no urine was passed; two points in close agreement with those of the first hemorrhage. The urine volume ran much higher after the second hemorrhage than after the first. In the four days following the second hemorrhage the average urine volume was 554 cc. (Table XII), while the average daily elimination for seven days was 525 cc. and for the whole 21 days of the experiment was 530 cc. When contrasted with the average of 451 cc. for the four days following the first hemorrhage and 489 cc., the average for the whole experiment, the variations are quite impressive. These volumes seem to indicate that the second hemorrhage was not so successful in masking the diuretic effect of the anaesthesia as was the first hemorrhage.

The body weight of the animal fell from 15.72k. to 15.18k. on the first day of the experiment, showing a loss of 0.54k. thus very closely agreeing with the loss of 0.51k. sustained through the agency of the first hemorrhage. The body weight continued to fall until, on the fourth day, a weight of 14.76k was registered. This weight was maintained practically unaltered for six days when another gradual decrease began and continued until the end of the experiment. The total loss of weight in the twenty-one days, exclusive of the loss due to hemorrhage, was 0.76k. The reaction of the urine was as a rule amphoteric during the early days of the experiment, the alkalinity gradually decreasing until, during the closing days of the experiment the amphoteric character had disappeared and an acid reaction obtained.

In agreement with the observations following the first hemorrhage the second day showed us a large volume of urine having the highest specific gravity of any urine of the experiment, and likewise containing the highest nitrogen content.

2. Discussion of the Income and Outgo of Nitrogen, Sulphur and Phosphorus After the Second Hemorrhage.—This experiment started with the dog approximately at nitrogen equilibrium, *i. e.*, showing daily loss of but 0.141 gram of nitrogen. The loss of blood caused this condition to rapidly change into one of largely increased nitrogen elimination and at the end of the seventh day a daily increase of 1.799 grams of nitrogen was noted. Making the proper correction for the influence of the anaesthetic (See p. 75)

we have, for the first seven days a daily increase of 2.736 grams of nitrogen as the combined effect of the operation and hemorrhage, and correcting further for the operation, we obtain a daily increase of 1.03 grams as the individual effect of the hemorrhage (Table XIX). It will be recognized that this increase was somewhat higher than the increase due to the first hemorrhage. The larger urine volume may have had some influence in this direction. The last five days of the experiment indicate a loss of 0.150 gram of nitrogen daily, comparing very favorably with the average loss of 0.141 gram at the beginning.

In agreement with the large increase in the nitrogen excretion following hemorrhage, the excretion of sulphur was also unusually high. This element showed an increase of 0.180 gram per day for the entire experiment (Table VI). The excretion of phosphorus, as usual, followed a course typically its own and instead of showing an increase as did the nitrogen and sulphur, it registered a decreased excretion amounting to 0.163 gram per day (Table VII).

VI. THIRD HEMORRHAGE.

The third hemorrhage occurred on the morning of Jan. 13, just 21 days after the second hemorrhage. The dog at this time was seemingly in fine condition and was using the leg, operated upon at the second hemorrhage, in a normal manner. It was decided to draw blood on this occasion from the left femoral artery slightly higher up than the site of the second hemorrhage.

The operation began at 8.20 A. M., the technique being analogous to that of former operations. Upon making the incision we were much surprised at the altered position of the femoral artery. Down beneath and around the wound of the second hemorrhage the central end of the artery was surrounded by a peculiar capsule formation which pushed upon the artery causing it to lie deeply imbedded among the tissues. After inserting the cannula the hemorrhage was allowed to continue ten minutes at the end of which period it was evident from physical signs that it would not be policy to continue the hemorrhage longer. The tongue of the beast was much more blanched than at previous hemorrhages and the pulse in the right femoral was almost imperceptible. The

animal was so very weak that the sewing up of the wound was hastened and the administration of ether discontinued as soon as possible. Thus the period of anaesthesia was somewhat shorter than at the previous operations. The wound of the second hemorrhage was drained, a few deep lying stitches were removed, and the whole wound cleansed with carbolic acid. A schedule of the operative steps follows:—8.20 A. M., anaesthesia begun. 8.28, trace of chloroform. 8.41, operation begun. 9.14, cannula inserted. 9.15, hemorrhage begun. 9.20, ether discontinued. 9.24, hemorrhage ended. 9.52, wound sewed up. 9.53, animal in cage. 10.02, returning consciousness. 10.20, dog sits up.

There was somewhat less salivation than at previous operations. A short time after the operation the dog used his leg much more handily than after former hemorrhages. The total blood lost to the organism aggregated 505.5 grams.

1. **Observations on the Influence of the Third Hemorrhage.**—A larger percentage of the total blood of the animal was drawn at this hemorrhage than upon any other occasion during the course of the experiments. As has been said the blood was allowed to flow until the animal was in an extremely weakened state. When the weights were made it was found that the total hemorrhage had been 505.5 grams or 3.51% of the body weight of the animal. According to the theory of Hammarsten (loc. cit.) a hemorrhage of 534 grams would have been fatal. We are inclined to believe that a short continuation of the hemorrhage would have been attended by fatal results; but, in view of the rapid recovery of the dog we do not believe that an increase of 28.5 grams in the amount of blood drawn would have caused the death of the animal. It was very evident, however, that the dog was much more effected by this third hemorrhage than by either of those preceeding it.

In some of the principal points the effects produced by the third hemorrhage corresponded very closely with those of the first and second hemorrhages. One of the most important factors, *i. e.*, the nitrogen excretion, showed the same characteristic of increased elimination. We also see upon the first day of the experiment the customary small volume of urine having a low specific gravity; although the difference between the urine volume of this day

and the volumes of the days following was not so great as was noted after the first two hemorrhages. The failure of the later days of this experiment to show the usual percentage increase over the volume of the first day is probably to be found in the variation in the time of anaesthesia. At each of the first two hemorrhages the beast was under the influence of the anaesthetic for approximately 2¼ hours; whereas at the third hemorrhage we were forced to limit the period of anaesthesia to somewhat less than 1¾ hours. Bearing in mind the diuretic effect traceable to the ether it is easily seen that a much larger urine volume might possibly have resulted had the anaesthesia continued the usual length of time.

The length of the period between the operation and the elimination of the first urine appeared to differ very decidedly from that of the previous hemorrhages. At the first and second hemorrhages no urine was passed until from 16 to 24 hours after the operation; whereas after the third hemorrhage the first elimination was in from 5 to 6 hours. By an examination of the data, however, we learn that the last urination preceeded the operation by 8 hours and that therefore ⅓ of the normal daily urine volume was probably in the dog's bladder at the time of the hemorrhage. Hence, under the circumstances, the passing of urine at an earlier hour was to have been expected. A second urination occurred between 16 and 24 hours after the operation and we think, therefore, that we are justified in considering the first urine passed as having been formed previous to the operation. The volume passed at this first urination was 180 cc. which at the same rate, would have given us a volume of 540 cc. for the entire 24 hours. This value would agree very closely with the average volume (530 cc.) for the experiment immediately preceeding.

The body weight of the dog fell from 14.42k. to 13.76k. after the hemorrhage, a loss of 0.66k., the greatest loss noted at any time during the 84 days of the investigation (Table XII).

2. **Discussion of the Income and Outgo of Nitrogen, Sulphur and Phosphorus After the Third Hemorrhage.**—The third hemorrhage took place after the animal had apparently entirely recovered from the effect of the second hemorrhage and was again in a condition of approximate nitrogen equilibrium. This condition was repre-

sented by a loss of 0.15 gram of nitrogen daily. Upon the day of the hemorrhage, as was also the case at each of the preceeding hemorrhages, the nitrogen content of the urine was the lowest of any day of the experiment. The second day, however, showed a very decided rise and the maximum was reached on the third day. The average nitrogen elimination was 11.669 grams daily, whereas for the five days preceeding the hemorrhage the dog eliminated an average of 10.421 grams daily. Therefore the hemorrhage and its associated influences caused an increased output of nitrogen amounting in the aggregate to 1.248 grams daily. It will be recognized that this was almost precisely the same as the combined influence of the anaesthesia, operation and hemorrhage at the first withdrawal of blood, the difference being but 0.009 gram. The increase in nitrogen after the second hemorrhage was somewhat greater and was probably due, in part, as has already been stated, to the cumulative diuretic effect of the anaesthesia which appreciably raised the urine volume. After the third hemorrhage, however, as we have seen, the anaesthetic having been administered for a shorter period, this large urine volume was not apparent but the average volume for the period was 53 cc. less than after the second hemorrhage and 12 cc. less than after the first hemorrhage (Table XII).

After making the proper correction for the influence of the anaesthesia (See p. 75) we secured 2.185 grams (Table XIX) as the increase in the nitrogen output due to the combined influence of the operation and loss of blood; and correcting further for the operation, we obtained as the net influence of the hemorrhage an increase of 0.479 gram in the daily nitrogen elimination. The balance for the last four days of the experiment (Table IV) showed an increase of 0.265 gram in the daily nitrogen elimination, while the data for the entire experiment, owing to the brevity of the period as well as to the greatly increased elimination of the first few days, showed a daily increase of 0.751 gram.

The excretion of sulphur apparently ran closely parallel with that of nitrogen, the sulphur balance indicating a daily increase of 0.229 gram (Table VI). The excretion of phosphorus on the other hand, in close agreement with the observations after the first and second hemorrhages, showed a gain of 0.065 gram for each day of the period (Table VII).

VII. FOURTH HEMORRHAGE.

By referring to the proper data it will be seen that the period between the third and fourth hemorrhages was much shorter than that between the first and second, or between the second and third. Furthermore it will be recognized that the fourth hemorrhage was instituted before the dog was as near a condition of nitrogen equilibrium as upon the former occasions. It will be remembered that after the first hemorrhage the dog was brought to nitrogen equilibrium in 16 days, whereas 21 days were necessary to secure a like result after the second hemorrhage. Gathering from these facts that it would probably take three weeks or longer to bring the organism to nitrogen equilibrium after the third hemorrhage, we decided to observe the influence of the hemorrhage over a small number of days, and, when we had secured approximate equilibrium, to follow with another hemorrhage. Then as we already had data for three hemorrhages when the dog was at nitrogen equilibrium, we decided at this point that an interesting study could be made of hemorrhages at short intervals upon this same animal, no attempt being made to secure nitrogen equilibrium. Therefore the period following the third hemorrhage was terminated, and the fourth hemorrhage produced, at a point where the dog was losing 0.265 gram of nitrogen daily.

At the time of the fourth hemorrhage the dog was able to walk about comfortably, but was not in as normal a condition as upon the occasion of the former hemorrhages. The right femoral artery just above the point at which the saphenous branch left it, was selected as the site of the hemorrhage. After 200 grams of blood had been drawn the arterial pressure was so low that only a slight flow was secured. The blood clotted very rapidly, necessitating frequent changes of the rubber tube. The body of the beast was freely massaged above the incision, and the cannula and rubber tube were frequently cleaned by means of a long platinum wire, but even after using the greatest efforts to secure the best conditions for a satisfactory hemorrhage a slow dropping was the maximum rate of flow. Thinking that perhaps the clot might extend back into the artery the platinum wire was frequently inserted for some distance into the vessel at the risk of puncture. After securing about 400 grams of blood the first cannula was removed

and a second one inserted a short distance above the first. Here however with fresh cannula and rubber tube the flow was not rapid enough to prevent clotting in both tube and cannula. The tube was discarded and blood collected directly from the cannula but the flow was not accelerated. It being evident that the hemorrhage had continued to a point where the arterial pressure was insufficient, the attempt to withdraw additional blood was abandoned. Therefore at 10.19 the administration of ether was discontinued, the wound sewed up and the animal returned to his cage. The usual schedule follows:—8.29 A. M., anaesthesia begun (ether). 8.37, trace of chloroform. 8.55, operation begun. 9.16, cannula inserted. 9.18, hemorrhage begun. 9.57, second cannula inserted to facilitate flow. 10.18, hemorrhage ended, making a total collection of 444.5 grams of blood. 10.19, second cannula out and ether stopped. Tongue extremely white. 10.31, wound sewed up. 10.36, in cage. 10.43, returning consciousness. 10.56, sits up. The period of anaesthesia of this experiment was two hours and fourteen minutes, being somewhat longer than that of the third hemorrhage and essentially the same as those of the first and second hemorrhages. There was practically no salivation at this operation.[1] The total blood lost to the organism was 449.3 grams.

1. Observations on the Influence of the Fourth Hemorrhage, with a Discussion of the Income and Outgo of Nitrogen, Sulphur and Phosphorus.—An interesting condition was noted after this hemorrhage for the first time during our experiments. This was a loss of appetite on the part of the dog. At the usual meal hour the animal was given his food, but contrary to custom, he ate very little of the mixture, and a large part of that eaten was water. About five minutes later he was again offered the food while he was lying down. This time he ate the entire amount, but did not evince his accustomed eagerness. The same lack of appetite was noted upon the next day also.

There was no excretion of urine for 12 hours after the hemorrhage (Table V). The urine volume on the day of the hemor-

[1] Preliminary to the operation the wound from the third hemorrhage was flushed and the collateral circulation noted.

rhage was 463 cc. (Table XII) and this was followed by a gradual rise until the maximum excretion of 770 cc. was reached on the third day. This volume was also the largest output of any day during the investigation. The usual decrease in body weight was noticed after this hemorrhage.

An examination of the data showed a greatly increased nitrogen excretion. This increase, after correcting for anaesthesia-operation, was 2.506 grams (Table XIX) and was about 5 times as great as that observed after the first and third hemorrhages and about 2½ times as great as that after the second hemorrhage. This evidently showed quite forcibly the cumulative effect of successive hemorrhages upon proteid catabolism.

The days following the hemorrhages gave an average increase of 0.348 gram in the sulphur elimination. In agreement with the nitrogen increase this increased excretion of sulphur was the largest of any period during the investigation.

For the first time the post hemorrhagic effect upon the phosphorus output was an increased elimination. There was an average daily increase of 0.180 gram (Tables VII and XIX).

VIII. FIFTH HEMORRHAGE.

No efforts were made to get the dog into nitrogen equilibrium after the fourth hemorrhage, it being thought best to determine the effect of another very severe hemorrhage before the organism had been given time to recover, in any great degree, from the loss of blood occasioned by the fourth hemorrhage.

The same procedure was followed as at the other hemorrhages, the blood being drawn from the right femoral artery above the point of the fourth hemorrhage.

No pulse could be felt at the point determined upon for the incision, but thinking the artery had changed position and become more deeply imbedded in the tissues the incision was made. After locating the artery it was found to be completely closed by a blood clot which extended some distance above the incision of the fourth hemorrhage. This necessitated another incision farther up.

It was determined to be guided entirely by the condition of the subject as to the amount of the hemorrhage, as the loss of blood was to be carried to the extreme limit.

After a hemorrhage of 317.5 grams or 2.46% of the body weight had been produced, it was very apparent, from the condition of the animal, that approaching death was indicated, and the flow of blood was suspended. The number of red corpuscles in the blood at this point was found to be 1,800,000 per cubic millimeter, thus indicating a very anaemic state.

In spite of very vigorous stirring in the presence of 25% NaCl solution, the blood, while possessing a very thin watery appearance as it flowed from the artery, soon coagulated. The whole mass was filled with light colored flakes due to the greatly increased number of leucocytes.

After being placed in his cage, and having recovered from the effect of the ether, the animal failed to show his habitual desire to sit up, but lay in a collapsed condition on the bottom of the cage. At 12 o'clock, two hours after the hemorrhage, his respiration was 9 and his pulse 152 per minute. At 1 P. M. 152 cc. of urine was passed having a specific gravity of 1.0255, much higher than any former urine had shown on the day of hemorrhage. At 4 P. M. his extremities were cold, axillary temperature was subnormal, and in spite of the greatest efforts to preserve his life the animal died 3 hours later.

1. **Post-mortem Examination.**—The bladder was removed and 14 cc. of urine with a specific gravity of 1.036 (the highest of any sample during the entire investigation) was secured. From our records it was learned that the dog urinated last at 1 P. M. and therefore this 14 cc. of urine represented the total urine formation for 6 hours. Ordinarily the animal would have passed over 100 cc. during a period of that length.

All of the animal's organs were extremely pale, and showed practically no tendency to bleed when cut. Even the heart was blanched and upon laying it open, a very small clot in the left ventricle was the only blood to be found.

In general the post-mortem examination showed conclusively that a very great portion of the animal's blood had been removed. As only about 300 cc. of blood was taken at the fifth hemorrhage, it was evident that the regeneration of the volume during the period since the fourth hemorrhage had been exceedingly slow.

C.—SECOND SERIES OF EXPERIMENTS.

This second series of experiments was much shorter than the first series and was made principally for the purpose of checking, upon another organism, the results from our first series. In this second series the experiments were made upon a dog weighing 11.85kg.

In our first series the influence of anaesthesia-operation was not determined until after the animal had been subjected to a preliminary hemorrhage. In the present series, however, after getting the organism into a condition of approximate nitrogen equilibrium by means of a preliminary period, the influence of anaesthesia-operation was studied before any blood was drawn. Following this, after returning to equilibrium, the effect of hemorrhage was studied.

The diet as shown by Table XV, was qualitatively the same as that of the first series of experiments.

I. Preliminary Experiment.

In a preliminary period of nine days, during which the dog was fed a constant diet, the organism was brought to approximate nitrogen equilibrium. For this period, as may be seen from an examination of Table XVI, there was an average daily loss of but 0.10 gram of nitrogen to the body. The organism was therefore in an exceptionally good condition for the study of the influence of anaesthesia-operation.

II. Influence of Anaesthesia-Operation.

As has been said, the influence of anaesthesia-operation in the first series of experiments was not determined until after the organism had been subjected to an initial hemorrhage. In order to secure additional data the influence of anaesthesia-operation was determined in the second series before the first hemorrhage.

As usual, the femoral artery was laid bare just above the point at which the saphenous branch is given off. The incision was longer and deeper than at any previous operation, in order to demonstrate to the full any influence exerted by this operative

procedure. The schedule of operations was as follows:—8.22 A. M., anaesthesia begun. 8.26, trace of chloroform given. 8.55, incision made. 9.20, wound sewed up. 9.45, returning consciousness. 10.00, dog sat up. This animal was evidently more susceptible to the influence of the ether than the former beast as was evidenced by the ease with which the preliminary anaesthesia was conducted as well as by the weakness of the animal after consciousness had returned.

The influence of anaesthesia-operation was studied through a period of nine days. Here as in the case of the first series of experiments, the anaesthesia-operation was followed by an immediate rise in the excretion of nitrogen by the urine. The average daily output of nitrogen by the urine, during the preliminary period was 7.73 grams (Table XVII). On the first day of the anaesthesia-operation period the nitrogen elimination was increased to 8.56 grams (Table XVII) and the average daily output for the first three days of the period was 9.12 grams. Taking the whole nine days into consideration the average daily output of nitrogen by the urine was 8.79 grams. The balance for the period showed a daily loss of 1.09 grams of nitrogen to the organism (Table XVI). At the beginning of the period the organism was losing 0.10 gram of nitrogen daily, and correcting for this we see that the net effect of the anaesthesia-operation upon the excretion of nitrogen has been to increase the output on an average 0.99 gram per day.

The general tendency of the sulphur excretion to follow a course similar to that of the nitrogen excretion was noted here. By means of the preliminary period of nine days the organism was placed in a condition of almost exact sulphur equilibrium, the average daily loss being 0.001 gram (Table XVIII). The influence of the anaesthesia-operation was shown in the form of an increased sulphur excretion. During this period the organism showed an average daily loss of 0.053 gram, thus signifying that the sulphur excretion was increased 0.052 gram daily as the effect of the anaesthesia-operation, or a total increase of 0.496 gram for the nine days.

As usual the phosphorus excretion showed a slight decrease as the effect of the anaesthesia-operation. The animal at the open-

ing of the period was losing 0.03 gram of phosphorus daily (Table XVIII). Under the influence of the anaesthesia-operation the phosphorus excretion decreased a trifle, making the average daily loss for the period 0.025 gram.

III. Influence of Hemorrhage.

Upon June 20 a hemorrhage was induced in the left femoral artery. The blood was withdrawn rapidly in this case, the total amount of blood taken aggregating 342.5 grams or 3.11% of the body weight of the animal. Due to the rapidity of the hemorrhage there were profound disturbances of pulse and respiration, but these were of short duration. The schedule of operations was as follows:—8.15 A. M., anaesthesia begun. 8.20, chloroform given. 8.35, operation begun. 8.50, cannula inserted. 8.53, hemorrhage begun. 9.00, hemorrhage ended. 9.02, cannula removed. 9.15, wound sewed up. 9.20, anaesthesia discontinued and dog returned to cage. 9.50, dog stood up.

In complete agreement with the data for the combined effect of hemorrhage and anaesthesia-operation in the first series of experiments, we also find here in the second series that a considerable increase in the excretion of nitrogen by the urine resulted. The average daily excretion of nitrogen was 9.47 grams for the period of five days following the hemorrhage (Table XVII). The nitrogen balance for this period showed an average daily loss of 1.88 grams (Table XVI). Correcting this for the normal daily loss of 0.10 gram, determined in the preliminary period, we find that the combined effect of hemorrhage and anaesthesia-operation has been to cause an average daily increase of 1.78 grams in the excretion of nitrogen. And correcting further for the influence of anaesthesia-operation (0.99 gram), we find that the withdrawal of 342.5 grams of blood[1] was instrumental in causing an average daily increase of 0.79 gram in the nitrogen excretion throughout a period of five days.

As usual the course of the sulphur excretion was similar to that of nitrogen, while the phosphorus excretion instead of being increased by the hemorrhage was slightly decreased (Table XVIII).

[1] The analysis of this blood was as follows: Nitrogen, 3.17 per cent.; sulphur, 0.156 per cent.; phosphorus, 0.48 per cent.

D.—ALTERATIONS IN THE SPECIFIC GRAVITY, AND IN THE NITROGEN, SULPHUR AND PHOSPHORUS CONTENT OF THE BLOOD FOLLOWING HEMORRHAGE.

The first and second hemorrhages being separated from each other by a period of nearly six weeks may be considered initial hemorrhages. That is, the composition of the blood drawn on Dec. 23 cannot be considered as the composition of the blood as effected by the hemorrhage of Nov. 14, for it is well known that the influence of a very severe hemorrhage would, so far as the composition of the blood is concerned, have disappeared long before the second hemorrhage. Hence the blood drawn on Dec. 23 may be considered normal blood.

Of the elements under consideration the nitrogen appeared to be the only one effected in any uniform manner by the successive hemorrhages. With this element beginning Dec. 23, which may be considered the commencement of the series of hemorrhages, we note, by referring to Table II, the normal nitrogen content of the blood to be 2.85%. Three weeks later the third hemorrhage showed a nitrogen content of 2.38%, while following this, after an interval of one week, the fourth hemorrhage gave us a nitrogen value of 1.848%, and after a short interval of four days at the fifth and final hemorrhage the minimum point was reached and the surprisingly low nitrogen value of 1.421% was recorded. Thus the effect of four successive hemorrhages in a period of one month on the nitrogen content of the blood had been to decrease the amount from 2.85% to 1.421%, a decrease of more than 50%. There was an actual decrease of 16% in the nitrogen content of the blood at the third hemorrhage, of 22% at the fourth hemorrhage and of 23% at the fifth hemorrhage. The time between the hemorrhages decreasing as it did from three weeks to only four days at the final hemorrhage, there seems to have been a very pronounced cumulative effect of some kind which produced in four days time a greater percentage decrease in the content of nitrogen than was previously secured after a lapse of three weeks.

The sulphur did not exhibit the same regularity as the nitrogen. It coincided, however, in showing the minimum output following the last hemorrhage. The content of phosphorus also was not governed by any uniformity, but differed radically from the nitrogen and sulphur in showing the maximum percentage at the last hemorrhage. Hence the maximum phosphorus occurred coincidently with the minimum sulphur, and the minimum phosphorus with the maximum sulphur (See analyses for fourth hemorrhage).

The specific gravity was lowered at each successive hemorrhage, falling from 1.0625 at the first hemorrhage to 1.047 at the fourth. The blood from the fifth hemorrhage showed a greatly increased specific gravity. This was due to the fact that the blood immediately after withdrawal, even in the presence of the 25% NaCl solution, showed a tendency to coagulate. This of course prevented the accurate determination of its specific gravity, and made the specific gravity as determined much too high. We are satisfied that the blood as drawn from the animal had a very low specific gravity as it was extremely thin and watery. Without doubt it was lower than that of any of the samples previously examined.

E.—RELATION BETWEEN TOTAL NITROGEN AND VOLUME OF URINE.

The ratio between the nitrogen content of the urine and the urine volume showed quite decided fluctuations under different experimental conditions. Starting with a ratio of 1:55.9 for the preliminary experiment (Table XIII), the first hemorrhage produced a very decided lowering of the ratio, the relation at this time being 1:45.8. During the latter part of the first hemorrhage experiment the ratio gradually rose and at the time nitrogen equilibrium had been reached it was 1:54.5.

The anaesthetic through its diuretic action now forced the ratio still higher, the maximum point being reached during the last days of the anaesthesia experiment. This was evidently due to the cumulative diuretic effect of the ether. From the result obtained

during the first days of the anaesthesia experiment we would naturally expect a rise in the ratio during the first days of the anaesthesia-operation experiment. Here, however, although the anaesthesia was of the same duration as before, instead of a rise we obtained a fall. This evidently indicated that the individual influence of the operation had been partly to overcome the rise due to anaesthesia. The ratio rose slightly higher during the following days of the experiment, but was at no time higher than the normal ratio of the preliminary experiment.

The second hemorrhage produced a corresponding fall to that observed after the first hemorrhage with a similar rise during the later days of the experiment. The third, fourth and fifth hemorrhages, while not strictly comparable with the first and second hemorrhages, each showed a low ratio, those of the fourth and fifth (1 :43.0 and 1 :40.3) being the lowest of the whole investigation. This rapid fall in the ratio after the fourth and fifth hemorrhages was evidently due to the fact that while the regenerative activities caused a large increase in proteid decomposition a corresponding increase in water output was impossible since the water content of the body had been so greatly decreased by the excessive blood-letting.

F.—DISCUSSION OF RESULTS.

The data from our experiments indicate that the loss of blood by an organism is followed immediately by an increased proteid catabolism. And furthermore, it was plainly demonstrated, by a series of hemorrhages on the same organism brought to a condition of nitrogen equilibrium before each loss of blood, that there is a tendency under such conditions for the catabolism of proteid to become more and more pronounced as the series progresses. This was shown by a daily increase of 1.257 grams in the nitrogen elimination as the result of a hemorrhage of 2.93% of the body weight of the animal, followed some weeks later by a daily increase of 3.275 grams in the nitrogen elimination after a hemorrhage of 3.26% of the body weight.

The influence of the anaesthesia to which the animal was subjected was to cause a daily *decrease* of 0.937 gram in the nitrogen output.[1] Another influencing factor was the operation which was shown of itself to cause an increased proteid catabolism, the average daily nitrogen elimination being increased 1.706 grams. Now taking the values named in the above paragraph as representing the gross influence of the hemorrhage, and correcting them for the influence of the anaesthesia and of the operation, we see that the net effect of the *hemorrhage alone* (Table XIX) was to cause a daily increase in the nitrogen elimination varying from 0.488 gram after a loss of blood amounting to 2.93% of the body weight, to 2.506 grams after a hemorrhage of 3.26% of the body weight.

The influence of the hemorrhage and its accompanying factors upon the excretion of sulphur was similar to that noted in the case of nitrogen. The daily increase in the sulphur excretion following hemorrhage varied from 0.023 gram to 0.348 gram, and the increase due to the anaesthesia-operation was 0.119 gram daily. The anaesthesia of itself caused a daily decrease of 0.128 gram in the sulphur excretion.

The phosphorus excretion, with a single exception, was influenced by hemorrhage and its associated factors in a manner directly opposite to that in which the nitrogen and sulphur excretions were influenced. In the case of the phosphorus the net influence of the *hemorrhage alone* was to cause a *decrease* in the elimination, the daily decrease varying from 0.163 gram to 0.065 gram. The anaesthesia-operation caused a daily decrease of 0.148 gram and the anaesthesia alone caused a daily *increase* of 0.108 gram. The decrease in the elimination of phosphorus after hemorrhage we believe to be due primarily to the unusual demands made upon nuclear material for the construction of leucocytes and nucleated erythrocytes.

Upon the day of the hemorrhage the urine volume was invariably sub-normal, but following this came a greatly increased output of urine which generally reached its maximum on the third or fourth day after the hemorrhage. This increase in the urine volume was partly due no doubt to the diuretic influence of the anaesthetic. Furthermore, the animal received a uniform supply

[1] Hawk: Proceedings of the American Physiological Society, 1903.

of water daily and this supply was sufficient for the dog under normal conditions as was witnessed by the promptness with which nitrogen equilibrium was reached. Upon withdrawing a large amount of blood, however, this normal water supply was more than sufficient for the needs of the altered metabolism, and therefore a portion of the excess was excreted. As was to have been expected this large urine volume was accompanied by an increased elimination of nitrogen, this increase being due in part to a flushing-out of the tissues as well as to a direct stimulation of proteid catabolism.[1]

The body weight of the animal decreased very materially on the day of the hemorrhage, the decrease being due apparently as much to the influence of the anaesthesia[2] as to the effect of the loss of blood.

The well konwn leucocytosis followed the hemorrhages and a decrease in the number of erythrocytes was also noted. As has already been stated on page 41, a most remarkable leucocytosis was observed at the time of the fifth hemorrhage.

The appetite of the subjects, with the single exception noted, (page 39), continued uniformly good throughout the experiments, even when the body weight of the animal had decreased very considerably. The regular normal diet which was just sufficient to bring the organism weighing about 17kg. to nitrogen equilibrium was very probably in excess of the needs of the body when the weight had been reduced to about 13kg. at the time of the fourth hemorrhage. Therefore this excessive amount of proteid material may have tended to stimulate proteid catabolism and thus assisted in the production of the maximum increase in the nitrogen elimination which was observed at that time.

G.—CONCLUSIONS.

1. Hemorrhages of 2.9% to 3.5% of the body weight upon dogs fed a constant diet and in a condition of nitrogen equilibrium, caused an increased urinary elimination of nitrogen and sulphur and a decreased elimination of phosphorus.

[1] Hawk: University of Pennsylvania Medical Bulletin, 1905, XVIII., 7.
[2] Hawk: Proceedings of the American Physiological Society, 1903.

2. Ether anaesthesia incident to ordinary surgical procedure was followed by a decreased elimination of nitrogen and sulphur and an increased elimination of phosphorus and chlorine.

3. The combined effect of the ether anaesthesia and the operative procedure was to cause an increased elimination of nitrogen, sulphur and chlorine and a decreased elimination of phosphorus.

4. After hemorrhages of 2.9% to 3.5% of the body weight there was an immediate decrease in the volume of urine. This decrease was followed after the first day by an increase and the maximum urine volume generally occurred on the third or fourth day after the hemorrhage.

5. Ether anaesthesia unaccompanied by loss of blood, produced an immediate diuresis which caused the maximum urine volume to appear upon the day of the anaesthesia.

6. Successive hemorrhages on the same organism caused a gradual decrease in the nitrogen and sulphur content of the blood, and a less regular decrease in the phosphorus content.

7. In a series of hemorrhages the specific gravity of the blood gradually decreased to the end of the series.

8. Repeated hemorrhages at intervals of from one to five weeks caused the coagulation rate of the blood to shorten very perceptibly, particularly at the end of the series.

9. A decrease in body weight followed hemorrhage.

10. There was a pronounced leucocytosis and a decrease in the number of erythrocytes after hemorrhage.

11. Hemorrhage caused no disturbance of the digestive functions and had no effect upon intestinal putrefaction.

The author wishes to express his sincere thanks to Prof. W. J. Gies under whose direction this investigation was conducted.

H.—BIBLIOGRAPHY.

1. Bauer: Zeitschrift für Biologie, 1872, VIII., p. 567.
   Münchener Medicinische Wochenschrift, 1892, 39, p. 537
2. Jürgensen: v. Ziemssen's Handbuch d. Allgemeine Therapie, 1880.
3. Maltschewsky: Thesis (Russian), 1892.
4. Ascoli and Draghi: Berliner Klinische Wochenschrift, 1900, 37, p. 1055.

5. Fränkel: Virchow's Archiv, 1876, LXVII.

6. v. Noorden: Lehrbuch der Pathologie des Stoffwechsels, Berlin, 1893.

7. Lukjanow: Zeitschrift für Phys. Chem. 1883, VIII., p. 336.

8. Gürber: Münchener Medicinische Wochenschrift, 1892, 39, pp. 416 and 605.

9. Autokonenko: Archives des sciences biologiques, 1893, II., p. 516.

10. Baumann: Journal of Physiology, 1903, 29, p. 18.

11. Luzet: Archives de physiologie normale et pathologique, 1891, 3, p. 455.

12. Vulpain: Comptes rendus des seances de l'academie des sciences, 1877, 84, p. 1279.

13. Hünerfauth: Virchow's Archiv, 1879, 76, p. 310.

14. Buntzen: Copenhagen, 1879, p. 56. Quoted by Jürgensen.

15. v. Lesser: Archiv für Anatomie und Physiologie (Physiologische Abtheilung), 1878, p. 74.

16. Lyon: Virchow's Archiv, 84. Quoted by Autokonenko.

17. Bizzozero and Salvioli: Arch. per le scienze mediche, IV., 12, p. 273.

18. Monassein: Tübingen, 1872, p. 41.

19. Tschoudnowsky: Thesis (Russian), 1869. Quoted by Autokonenko.

20. Rieder: Beiträge zur Kenntniss der Lencocytosis und verwandter zustande des Blutes, 1892, p. 90.

21. Hayem: Lecons sur les modifications du sang, Paris, 1882.

22. Himmelstjerna: Dissertation, 1882, p. 25. Quoted by Autokonenko.

23. Virchow: Die Cellularpathologie, Berlin, 1862.

24. Limbeck: Grundriss einen clinischen pathologie des Blutes, 1892, p. 49.

25. Molassez: Gazette Médicale de Paris, 1880, II., p. 465.

26. Henle: Quoted by Jürgensen and Autokonenko.

27. Remak: Quoted by Jürgensen and Autokonenko.

28. Woltersom: Quoted by Donders, Phys. des Menschen, I., p. 166. Quoted by Bauer.

29. Conheim:
30. Massart and Bordet:
31. Gabritschewsky:
32. Afanasiew:
33. Leber:
34. Roemer:
35. Buchner:
36. Escherich:
37. Foster:
Quoted by Autokonenko.

38. Leichtenstern: Zeitschrift für Biologie, 1868, VII., p. 215.

39. Kussmaul and Tenner: Frankfort, 1857. Quoted by Bauer and Jürgensen.

40. Naunyn and Quinke: Du Bois Reymond's Archiv, 1869, Heft 2.

41. Gies: American Journal of Physiology, 1903, IX., p. 13.

42. Worm-Muller: Berichte der Sächsischen Gesellschaft der Wissenschaften, 1873, p. 642.
43. Volkmann: Die Hämodynamik, p. 197.
44. Nawrotzky:
45. Magendie: Quoted by Bauer.
46. Nawlichen:
47. Hayem: Loc. cit.
48. Hall: Quoted by Liebermeister in v. Ziemmsen's Handbuch, 1880, I.
49. Traube: Quoted by Bauer.
50. Spielman:
51. Frese and Charaszewski: Quoted by Jürgensen.
52. Wunderlich:
53. Brücke: Virchow's Archiv, 1857, XII., p. 179.
54. Nasse: Das Blut, Bonn, 1836, p. 156.
55. Jürgensen: Loc. cit.
56. Mayer: Quoted by Jürgensen.
57. Vierordt: Archiv der Heilkunde, XIX., p. 193.
58. Brücke: Loc. cit.
59. Nasse: Loc. cit.
60. Baumann: Loc. cit.
61. Sherrington and Copeman: Journal of Physiology, 1893, XIV, p. 52.
62. Otto:
63. Jones: Quoted by Sherrington and Copeman.
64. Bizzozero and Salvioli: Loc. cit.
65. Woltersom: Loc. cit. Quoted by Vierordt.
66. Baumann: Loc. cit.
67. Tolmatscheff: Medicinische Chem. Untersuchungen herausgegeben von Hoppe-Seyler, Tübingen, III., p. 400.
68. Bauer: Loc. cit.
69. Jürgensen: Loc. cit.
70. Lister: Quoted by Jürgensen.
71. Hünerfauth: Loc. cit.
72. Goll: Zeitschrift für Rationelle Medicin, Neue Folge, 1854, IV., p. 78.
73. Schramm: Medic. Jahrbücher, Wien, 1885, p. 492.
74. v. Kireeff: Archiv für Anatomie und Physiologie (Physiologische Abtheilung), 1884, p. 156.
75. Hayem: Loc. cit.
76. Noll: Quoted by Kronecker.
77. Kronecker: Correspondenzblatt für Schweizer Aerzte, 1886, 16.
78. Ott: Thesis (Russian), 1884, p. 32.
79. Maydl: Medic. Jahrbücher, Wien, 1884, p. 77.
80. Schramm: Loc. cit.
81. Prevost and Dumas: Quoted by Maydl.
82. Skvortsov: Inaugural Dissertation, St. Petersburg, 1890. Quoted in Bulletin 45, Office of Experiment Stations, Department of Agriculture, U. S. A.

83. Debierre and Linossier: Bulletin Général de Therapeutique, 1885, CVIII, p. 167.

84. Emminghaus: Ber. uber d. Verhandl. d. König. Sächs; Gesellsch. d. Wiss. Z. Leipzig, 1873, XXV.

85. Fleischer and Penzoldt: Deutsches Archiv für Klinische Medicin, 1880, XXVI., p. 400.

86. Lipmann-Wulf: v. Noorden's Beitrage zur Lehre vom Stoffwechsel, 1892, I., 24.

87. Ketcher: Vrach, 11, p. 1042. Quoted in Bulletin 45 (loc. cit).

88. Moraczewski: Zeitschrift für Klinische Medicin, 1897, 33.

89. Eichorst: Die progress. pernic. Anämie, Leipzig, 1878, p. 205. Quoted by v. Noorden.

90. Burzhinski: Vrach, 10, p. 994. Quoted in Bulletin 45, (loc. cit).

91. Sticker: Zeitschrift für Klinische Medicin, 1888, 14.

92. Albrecht: Jahrbuch für Kinderheilkunde, 1882, 18, p. 1.

93. Hayem: Loc. cit.

94. Rieder: Loc. cit.

95. Hayem: Loc. cit.

96. Samuel: Manuel de pathologie gènèral, 1879, p. 254.

97. King: American Journal of the Medical Sciences, 1902, CXXIV., p. 450.

98. Mosler: Leukämie. Quoted by Bauer.

99. Lowit: Virchow's Archiv, 117, p. 569.

100. Müller: Deutches Archiv für Klinische Medicin, 1901, 48.

101. Osler: Osler's Practice of Medicine, p. 789.

102. V. Noorden: Loc. cit.

103. Neusser: Wiener Klinische Wochenschrift, 1897, 10, p. 629. Quoted by Kolisch.

104. Kolisch: Wiener Klinische Wochenschrift, 1897, 26, p. 628.

I.—BIOGRAPHICAL.

Philip Bovier Hawk graduated from Wesleyan University in 1898 with the degree of Bachelor of Science. During the next two years (1898-1900) he was assistant to Prof. W. O. Atwater of Wesleyan University. During this time he also did graduate work in the University and received the degree of Master of Science in 1900. As a university scholar, in 1900-1901, he pursued graduate studies in physiological chemistry and physiology in Yale University and in 1902 received the degree of Master of Science from that institution. He served as assistant in physi-

ological chemistry in Columbia University (College of Physicians and Surgeons) during 1901-1903, at the same time pursuing graduate work in physiological chemistry. In 1903 the degree of Doctor of Philosophy was conferred upon him by Columbia University.

He is a member of Delta Kappa Epsilon, Sigma Xi, the American Physiological Society and the Society for Experimental Biology and Medicine.

J.—PUBLICATIONS.

1. On the elimination of nitrogen, sulphates and phosphates after the ingestion of proteid food (with H. C. Sherman); American Journal of Physiology, 1900, IV., p. 25.

2. Chemical studies of osseomucoid, with determinations of the heat of combustion of some connective tissue glucoproteids (with W. J. Gies); American Journal of Physiology, 1901, V., p. 387.

3. On the composition and chemical properties of osseoalbumoid, with a comparative study of the albumoid of cartilage (with W. J. Gies); American Journal of Physiology, 1902, VII., p. 340.

4. On the quantitative determination of acid albumin in digestive mixtures (with W. J. Gies); American Journal of Physiology, 1902, VII., p. 460.

5. On the influence of rennin upon the digestion of the proteid constituents of milk; American Journal of Physiology, 1903, X., p. 37.

6. On the time relations of proteid metabolism; American Journal of Physiology, 1903, X., p. 115.

7. A study in the course of the nitrogen, sulphate and phosphate excretion, as observed in short periods following a small increase in the proteid ingested (with Joseph S. Chamberlain); American Journal of Physiology, 1904, X., p. 269.

8. On the morphological changes in the blood after muscular exercise; American Journal of Physiology, 1904, X., p. 384.

9. On the influence of external hemorrhage on chemical changes in the organism, with particular reference to proteid catabolism (with W. J. Gies); American Journal of Physiology, 1904, XI., p. 171.

10. On the influence of copious water drinking; University of Pennsylvania Medical Bulletin, 1905, XVIII., p. 7.

TABLE I.—DAILY DIET (First Series).

Constituent of the Diet.		Am't in grams.	NITROGEN.						SULPHUR.						PHOSPHORUS.					
			Nov. 2–Dec. 4.		Dec. 5–Jan. 2.		Jan. 3–Jan. 24.		Nov. 2–Dec. 4.		Dec. 5–Jan. 2.		Jan. 3–Jan. 24.		Nov. 2–Dec. 4.		Dec. 5–Jan. 2.		Jan. 3–Jan. 24.	
			Per cent.	Grams.	Per cent.	Grams.	Per cent.	Grams.	Per cent.	Grams.	Per cent.	Grams.	Per cent.	Grams.	Per cent.	Grams.	Per cent.	Grams.	Per cent.	Grams.
Beef....	No. 1	250.0	3.670	9.175	....	....	....	....	0.2792	0.698	....	....	....	....	0.2229	0.557	....	....	....	....
	No. 2	256.4	....	....	3.578	9.175	....	....	....	....	0.3023	0.775	....	....	. ..	....	0.2178	0.558	....	....
	No. 3	241.0	....	....	....	. ..	3.806	9.175	....	....	....	....	0.2514	0.606	....	....	....	....	0.2185	0.527
			Per cent.			Grams.			Per cent.			Grams.			Per cent.			Grams.		
Cracker Dust		70	1.55			1.085			0.1318			0.092			0.1345			0.094		
Lard		30	0.028			0.008			0.03			0.009			0.085			0.026		
Bone Ash....		10	0.026			0.003			0.06			0.006			17.79			1.779		
Water............		500	.....			.....			.....			.....			.....			.....		
Total	Nov. 2–Dec. 4	860.0	.....			10.271			.....			0.805			.....			2.456		
	Dec. 5–Jan. 2	866.4	.....			10.271			.....			0.882			.....			2.457		
	Jan. 3–Jan. 24	851.0	.....			10.271			.....			0.713			.....			2.426		

TABLE II.—BLOOD ANALYSIS.

Date of hemorrhage.	Body weight of dog.	Total amount of blood taken.	Specific gravity.	Percentage of body weight.	Nitrogen.		Sulphur.		Phosphorus.	
					Per cent.	Grams.	Per cent.	Grams.	Per cent.	Grams.
1902	Kilograms.	Grams.								
Nov. 14	16.80	492.9	1.0625	2.93	2.591	12.769	0.138	0.682	0.045	0.222
Dec. 23	15.72	506.0	1.062	3.22	2.850	14.446	0.134	0.677	0.040	0.204
1903										
Jan. 13	14.42	505.5	1.058	3.51	2.318	11.720	0.134	0.677	0.040	0.203
Jan. 20	13.77	449.3	1.047	3.26	1.848	8.302	0.144	0.648	0.037	0.165
Jan. 24	12.90	317.5	1.069	2.46	1.421	4.512	0.124	0.393	0.043	0.135
Totals ...		2271.2				51.749		3.077		0.929

TABLE III.—SUMMARY OF NITROGEN BALANCES.

General Balances for Complete Experiments (First Series).

Experiment.	Date.	Days.	Income (grams). Diet. Nitrogen. Day.	Income (grams). Diet. Nitrogen. Period.	Outgo (grams). Urine. Nitrogen. Day.	Outgo (grams). Urine. Nitrogen. Period.	Outgo (grams). Feces. Nitrogen. Day.	Outgo (grams). Feces. Nitrogen. Period.	Outgo (grams). Hair. Nitrogen. Day.	Outgo (grams). Hair. Nitrogen. Period.	Outgo (grams). Washings. Nitrogen. Day.	Outgo (grams). Washings. Nitrogen. Period.	Outgo (grams). Total. Nitrogen. Day.	Outgo (grams). Total. Nitrogen. Period.	Gain or Loss. (Grams) Day.	Gain or Loss. (Grams) Period.
Preliminary...	Nov. 2-13, 1902	12	10.271	123.252	8.740	104.84	0.590	7.09	0.190	2.29	0.153	1.83	9.673	116.05	+0.59	+ 7.202
First hemorrhage .... (2.93 per cent.)	Nov. 14-29	16	10.271	164.336	9.54	152.68	0.560	8.96	0.200	3.27	0.15	2.39	10.450	167.30	—0.179	— 2.964
Anaesthesia...	Nov. 30—Dec. 9	10	10.271	102.710	8.957	89.57	0.581	5.81	0.175	1.75	0.197	1.97	9.910	99.10	+0.361	+ 3.61
Anaesthesia—operation ...	Dec. 10-22	13	10.271	133.523	9.900	128.71	0.580	7.55	0.147	1.91	0.195	2.54	10.822	140.71	—0.551	— 7.187
Second hemorrhage .... (3.22 per cent.)	Dec. 23—Jan. 12, 1903	21	10.271	215.691	10.470	219.91	0.587	12.32	0.160	3.36	0.164	3.44	11.381	239.03	—1.11	—23.339
Third hemorrhage .... (3.51 per cent.)	Jan. 13-19	7	10.271	71.897	10.176	71.23	0.562	3.935	0.144	1.01	0.140	0.95	11.022	77.125	—0.751	— 5.228
Fourth hemorrhage .... (3.26 per cent.)	Jan. 20-23	4	10.271	41.084	12.922	51.69	0.607	2.427	0.137	0.546	0.145	0.582	13.811	55.245	—3.540	—14.161

TABLE IV.—SUMMARY OF NITROGEN BALANCES (FIRST SERIES).

SHOWING { (1.) EXACT CONDITION OF THE ORGANISM AT THE BEGINNING OF EACH EXPERIMENT. (2.) MAXIMUM EFFECT SECURED IN EACH EXPERIMENT.

Period.	Date.	Days	Income (Grams). Diet. Nitrogen. Day.	Income (Grams). Diet. Nitrogen. Period.	Outgo (Grams). Urine. Nitrogen. Day.	Urine. Nitrogen. Period.	Feces. Nitrogen. Day.	Feces. Nitrogen. Period.	Hair. Nitrogen. Day.	Hair. Nitrogen. Period.	Washings. Nitrogen. Day.	Washings. Nitrogen. Period.	Total. Nitrogen. Day.	Total. Nitrogen. Period.	Gain or Loss. (Grams.) Day.	Gain or Loss. (Grams.) Period.
Before first hemorrhage	Nov. 9–13, 1902	5	10.271	51.355	9.090	45.48	0.590	2.950	0.190	0.950	0.153	0.765	10.023	50.145	+0.248	+ 1.21
After first hemorrhage. ...... (2.93 per cent.)	Nov. 14–18	5	10.271	51.355	10.370	51.84	0.560	2.800	0.200	1.000	0.150	0.750	11.280	56.390	—1.009	— 5.035
Before anaesthesia............	Nov. 25–29	5	10.271	51.355	9.520	47.62	0 560	2.800	0.200	1.000	0.150	0.750	10 430	52.170	—0.159	— 0.815
After anaesthesia........	Nov. 30–Dec. 3	4	10.271	41.084	8.540	34.17	0.581	2.324	0.175	0.700	0.197	0.788	9.493	37.982	+0.778	+ 3.102
Before anaesthesia —operation	Dec. 6–9	4	10.271	41.084	9.160	36.64	0.581	2.324	0.175	0 700	0.197	0.788	10.113	40.452	+0.158	+ 0.632
After anaesthesia —operation	Dec. 10–14	5	10.271	51.355	9.960	49.78	0.580	2 900	0.147	0.735	0.195	0 975	10 882	54.390	—0.611	— 3.035
Before second hemorrhage ..	Dec. 19–22	4	10.271	41.084	9.490	37.96	0.580	2.320	0.147	0.588	0.195	0.780	10.412	41.648	—0 141	— 0.564
After second hemorrhage .. (3.22 per cent.)	Dec. 23–29	7	10.271	71.897	11.300	79.12	0.587	4.109	0.160	1.120	0.164	1.148	12.211	85.497	—1.94	—13.60
Before third hemorrhage ..	Jan. 8–12, 1903	5	10.271	51.355	9.510	47.56	0.587	2.935	0.160	0.800	0.164	0.820	10.421	52.115	—0.150	— 0.760
After third hemorrhage .... (3.51 per cent.)	Jan. 13–15	3	10.271	30.813	10.823	32.47	0.562	1.686	0.144	0.432	0.140	0.420	11.669	35.008	—1.398	— 4.195
Before fourth hemorrhage ..	Jan. 16–19	4	10.271	41.084	9.690	38.76	0.562	2.248	0.144	0.576	0.140	0.560	10.536	42.144	—0.265	— 1.060

TABLE V.—ELIMINATION OF URINE

As Influenced by Anaesthesia and Hemorrhage

Experiment.	Date.	Time Begun.	First urine passed.	Hours after operation first urine was passed.	Volume of urine, cc.	Remarks-
	1902	a. m.	p. m.			
First hemorrhage .... (2.93 per cent.)	Nov. 14	8.10	Between Midnight and 8.30 a. m. (Nov. 15th)	16—24	300	
Anaesthesia...	Nov. 30	9 10	4.15	7	283	
Anaesthesia — operation ...	Dec. 10	8.12	4.20	8	294	
Second hemorrhage .... (3.22 per cent.)	Dec. 23	8.14	Between Midnight and 9 a. m. (Dec. 24)	16—25	590	
Third hemorrhage ...... (3 51 per cent.)	1903 Jan. 13	8.20	1-2	5—6	180	No urine 8 hours before the operation. Hence the major portion of the 180 cc. passed between 1 p. m. and 2. p. m. was evidently in the bladder at the time of operation.
Fourth hemorrhage .... (3.26 per cent.)	Jan. 20	8.29	8.30	12	200	No more urine until after 1 p. m. Jan. 21st.
Fifth hemorrhage ...... (2.46 per cent.)	Jan. 24	8.30	2.20	6	152	

TABLE VI.—SUMMARY OF SULPHUR BALANCES.

General Balances for Complete Experiments (First Series).

Experiment.	Date.	Days.	Income (Grams). Diet. Sulphur. Day.	Income (Grams). Diet. Sulphur. Period.	Outgo (Grams). Urine. Sulphur. Day.	Outgo (Grams). Urine. Sulphur. Period.	Outgo (Grams). Feces. Sulphur. Day.	Outgo (Grams). Feces. Sulphur. Period.	Outgo (Grams). Hair. Sulphur. Day.	Outgo (Grams). Hair. Sulphur. Period.	Outgo (Grams). Washings. Sulphur. Day.	Outgo (Grams). Washings. Sulphur. Period.	Outgo (Grams). Total. Sulphur. Day.	Outgo (Grams). Total. Sulphur. Period.	Gain or Loss. (Grams) Day.	Gain or Loss. (Grams) Period.
Preliminary ..	Nov. 2–13, 1902	12	0.805	9.660	0.445	5.339	0.187	2.244	0.024	0.294	0.014	0.170	0.670	8.047	+ 0.135	+ 1.613
First hemorrhage .... .. (2.93 per cent.)	Nov. 14–29	16	0.805	12.880	0.577	9.240	0.209	3.340	0.027	0.439	0.015	0.249	0.828	13.268	— 0.023	— 0.388
Anaesthesia...	Nov. 30–Dec. 9	10	0.844	8 435	0.517	5.167	0.187	1.871	0.020	0.201	0.015	0.150	0.739	7.389	+ 0.105	+ 1.046
Anaesthesia—operation ...	Dec. 10–22	13	0.882	11.466	0.655	8.517	0.208	2.701	0.019	0.247	0.014	0.185	0.896	11.650	— 0.014	— 0.184
Second hemorrhage....... (3.22 per cent.)	Dec. 23–Jan. 12, 1903	21	0.801	16.832	0.725	15.230	0.219	4.618	0.019	0.410	0.018	0.386	0.981	20.644	— 0.180	— 3.812
Third hemorrhage .... (3.51 per cent)	Jan. 13–19	7	0.713	4.991	0.699	4.892	0.207	1.450	0.018	0.126	0.018	0.126	0.942	6.594	— 0.229	— 1.603
Fourth hemorrhage .... (3.26 per cent.)	Jan. 20–23	4	0.713	2.852	0.794	3.174	0.225	0.890	0.017	0.068	0.025	0.103	1.061	4.235	— 0.348	— 1.383

TABLE VII.—SUMMARY OF PHOSPHORUS BALANCES.

General Balances for Complete Experiments (First Series).

Experiment.	Date.	Days.	Income (grams). Diet. Phosphorus. Day.	Income (grams). Diet. Phosphorus. Period.	Outgo (grams). Feces. Phosphorus. Day.	Feces. Phosphorus. Period.	Urine. Phosphorus. Day.	Urine. Phosphorus. Period.	Hair. Phosphorus. Day.	Hair. Phosphorus. Period.	Washings. Phosphorus. Day.	Washings. Phosphorus. Period.	Total. Phosphorus. Day.	Total. Phosphorus. Period.	Gain or Loss. (grams.) Day.	Gain or Loss. (grams.) Period.
Preliminary ..	Nov. 2–13, 1902	12	2.456	29.472	1.860	22.300	0.464	5.572	0.072	0.862	0.015	0.187	2.411	28.921	+ 0.045	+ 0.551
First hemorrhage .... (2.93 per cent.)	Nov. 14–29	16	2.456	39.296	1.790	28.670	0.521	8.332	0.008	0.132	0.014	0.222	2.333	37.356	+ 0.123	+ 1.940
Anaesthesia...	Nov. 30–Dec. 9	10	2.457	24.565	1.940	19.400	0.478	4.784	0.007	0.069	0.017	0.165	2.442	24.418	+ 0.015	+ 0.147
Anaesthesia—operation ...	Dec. 10–22	13	2.457	31.941	1.820	23.680	0.452	5.874	0.007	0.088	0.015	0.196	2.294	29.838	+ 0.163	+ 2.103
Second hemorrhage ...... (3.22 per cent.)	Dec. 23–Jan. 12, 1903	21	2.442	51.287	1.890	39.720	0.508	10.678	0.007	0.155	0.015	0.305	2.420	50.858	+ 0.022	+ 0.429
Third hemorrhage .... (3.51 per cent.)	Jan. 13–19	7	2.426	16.982	1.873	13.110	0.467	3.270	0.007	0.051	0.014	0.098	2.361	16.529	+ 0.065	+ 0.453
Fourth hemorrhage .... (3.26 per cent.)	Jan. 20–23	4	2.426	9.704	1.998	7.995	0.587	2.348	0.006	0.025	0.015	0.061	2.606	10.429	— 0.18	— 0.725

TABLE VIII.—AMOUNT AND COMPOSITION OF FECES.

Experiment.	Date.	No. of days.	Amount. (dry) (grams)	Nitrogen (grams).		Sulphur (grams).		Phosphorus (grams).	
				Per day.	Total.	Per day.	Total	Per day.	Total.
Preliminary	Nov. 2–13, 1902	12	224.4	0.590	7.09	0.187	2.244	1.860	22.300
First hemorrhage	Nov. 14–29	16	280.5	0.560	8.96	0.209	3.340	1.790	28.670
Anaesthesia	Nov. 30–Dec. 9	10	194.3	0.581	5.81	0.187	1.871	1.940	19.400
Anaesthesia–operation	Dec. 10–22	13	237.5	0.580	7.55	0.208	2.701	1.820	23.680
Second hemorrhage ..	Dec. 23–Jan. 12 1903	21	417.6	0.587	12.32	0.219	4.618	1.890	39.720
Third hemorrhage ...	Jan. 13–19	7	130.9	0.562	3.94	0.207	1.450	1.873	13.110
Fourth hemorrhage ..	Jan. 20–23	4	75.5	0.607	2.43	0.225	0.890	1.998	7.995

TABLE IX.—AMOUNT AND COMPOSITION OF HAIR.

Experiment.	Date.	No. of days.	Amount. (grams)	Nitrogen (grams).		Sulphur (grams).		Phosphorus (grams).	
				Per day.	Total.	Per day.	Total.	Per day.	Total.
Preliminary	Nov. 2–13, 1902	12	22.9	0.190	2.29	0.024	0.294	[1] 0.072	[1] 0.862
First hemorrhage	Nov. 14–29	16	24.6	0.200	3.27	0.027	0.439	0.008	0.132
Anaesthesia	Nov. 30–Dec. 9	10	12.9	0.175	1.75	0.020	0.201	0.007	0.069
Anaesthesia-operation	Dec. 10–22	13	14.8	0.147	1.91	0.019	0.247	0.007	0.088
Second hemorrhage..	Dec. 23–Jan. 12 1903	21	25.3	0.160	3.36	0.019	0.410	0.007	0.155
Third hemorrhage ...	Jan. 13–19	7	7.61	0.144	1.01	0.018	0.126	0.007	0.051
Fourth hemorrhage ..	Jan. 20–23	4	4.12	0.137	0.55	0.017	0.068	0.006	0.025

[1] Phosphorus content high here, due to presence of feces which in succeeding experiments was separated from the hair.

TABLE X.—VOLUME AND COMPOSITION OF WASHINGS.

Experiment.	Date.	No. of days.	Volume. (cc.)	Nitrogen (grams).		Sulphur (grams).		Phosphorus (grams).	
				Per day.	Total.	Per day.	Total.	Per day.	Total.
Preliminary	Nov. 2–13, 1902	12	2800	0.153	1.83	0.014	0.170	0.015	0.187
First hemorrhage	Nov. 14–29	16	2800	0.150	2.39	0.015	0.249	0.014	0.222
Anaesthesia	Nov. 30–Dec. 9	10	3600	0.197	1.97	0.015	0.150	0.017	0.165
Anaesthesia-operation	Dec. 10–22	13	3000	0.195	2.54	0.014	0.185	0.015	0.196
Second hemorrhage ..	Dec. 23–Jan. 12 1903	21	3800	0.164	3.44	0.018	0.386	0.015	0.305
Third hemorrhage ...	Jan. 13–19	7	3600	0.140	0.95	0.018	0.126	0.014	0.098
Fourth hemorrhage ..	Jan. 20–23	4	2200	0.145	0.58	0.025	0.103	0.015	0.061

TABLE XI.—SULPHUR AND PHOSPHORUS CONTENT OF URINE.

Experiment.	Date.	No. of days.	Average urine volume. (cc.)	Sulphur (grams).		Phosphorus (grams)	
				Per day.	Total.	Per day.	Total.
Preliminary	Nov. 2–13, 1902	12	489	0.445	5.339	0.464	5.572
First hemorrhage .... (2.93 per cent.)	Nov. 14–29	16	489	0.577	9.240	0.521	8.332
Anaesthesia	Nov. 30–Dec. 9	10	522	0.517	5.167	0.478	4.784
Anaesthesia-operation	Dec. 10–22	13	531	0.655	8.517	0.452	5.874
Second hemorrhage .. (3.22 per cent.)	Dec. 23–Jan. 12 1903	21	530	0.725	15.230	0.508	10.678
Third hemorrhage ... (3.51 per cent.)	Jan. 13–19	7	477	0.699	4.892	0.467	3.270
Fourth hemorrhage .. (3.26 per cent.)	Jan. 20–23	4	554	0.794	3.174	0.587	2.348

TABLE XII.

Daily Data of the First Series of Experiments.

I. Preliminary Experiment, Nov. 2–13, 1902

Day No.	Body-weight.	Urine.					Feces.	
		Volume.	Specific gravity.	Nitrogen.	Period average to date.		Weight.	
					Volume.	Nitrogen.	Fresh.	Dry.
	kilos	cc.		grams	cc.	grams	grams	grams
1	16.96	499	1017	8.30	499	8.30	46.5	24.4
2	16.96	581	1019	10.23	540	9.26	....	...
3	16.96	394	1021	7.82	491	8.78	43.1	22.1
4	16.95	499	1020	9.84	493	9.05	35.8	19.7
5	16.92	461	1020	8.56	487	8.95	27.8	15.6
6	16.89	445	1020	8.10	480	8.81	71.1	36.4
7	17.01	400	1018	6.51	468	8.48	....	...
8	16.78	662	1018	11.27	493	8.83	54.1	38.1
9	16.91	436	1018	7.33	486	8.66	32.4	18.2
10	16.83	443	1019	7.71	482	8.57	30.6	17.7
11	16.85	486	1019	8.57	482	8.57	32.3	17.8
12	16.80	560	1019	10.60	489	8.74	27.2	14.4
II. First Hemorrhage, (2.93 per cent.) Nov. 14–29, 1902								
13	16.29	377	1017	6.33	377	6.33	34.3	20.2
14	16.20	556	1027	13.34	467	9.84	..	...
15	16.20	501	1022	10.87	478	10.18	36.1	20.5
16	16.25	370	1022	7.63	451	9.54	69.1	34.1
17	16.20	570	1025	13.67	475	10.37	...	...
18	16.32	307	1017	5.25	447	9.51	45.3	23.1
19	16.37	475	1022	9.84	451	9.56	33.6	20.0
20	16.33	586	1021	11.40	468	9.79	38.2	19.0
21	16.34	462	1020	9.69	467	9.78	41.8	27.5
22	16.33	512	1019	8.84	472	9.69	...	...
23	16.32	520	1018	8.20	476	9.55	37.5	19.5
24	16.28	498	1019	9.41	478	9.54	37.1	20.7
25	16.29	463	1021	9.28	477	9.52	35.8	17.4
26	16.27	444	1019	7.56	474	9.38	42.5	21.6
27	16.18	576	1019	10.33	481	9.44	40.3	20.0
28	16.09	615	1020	11.04	489	9.54	32.8	16.9
III. Anaesthesia, Nov. 30–Dec. 9, 1902								
29	15.81	654	1018	8.59	654	8.59	64.0	35.9
30	15.85	495	1021	8.56	575	8.58	...	...
31	15.88	467	1019	8.80	539	8.65	36.2	20.1
32	16.02	388	1021	8.22	501	8.54	31.3	16.7
33	16.03	512	1020	10.70	503	8.97	59.3	32.6
34	16.09	458	1019	8.06	496	8.82	...	...
35	16.00	570	1018	9.01	506	8.85	64.0	36.4
36	16.00	555	1018	8.78	512	8.84	32.6	17.3
37	15.98	593	1017	9.20	521	8.88	...	...
38	15.94	532	1020	9.65	522	8.96	71.9	35.3

TABLE XII (*Continued*)

IV. Anaesthesia—Operation, Dec. 10-22, 1902

Day No.	Body-weight.	Urine.					Feces.	
		Volume.	Specific gravity.	Nitrogen.	Period average to date.		Weight.	
					Volume.	Nitrogen.	Fresh.	Dry.
	kilos	cc.		grams	cc.	grams	grams	grams
39	15.44	754	1018	9.98	754	9.98	40.0	20.5
40	15.42	572	1020	10.72	663	10.35	...	...
41	15.64	330	1019	6.73	552	9.15	35.2	19.0
42	15.67	520	1024	12.28	544	9.93	28.1	15.5
43	15.68	530	1020	10.07	541	9.96	63.4	35.4
44	15.68	596	1018	9.27	550	9.84	...	...
45	15.72	400	1019	7.77	529	9.55	41.9	21.7
46	15.69	558	1020	11.12	533	9.75	118.8	51.4
47	15.68	526	1023	12.81	532	10.09	...	...
48	15.66	556	1021	10.87	534	10.16	21.3	15.7
49	15.74	405	1018	7.41	522	9.91	32.5	15.7
50	15.70	575	1018	9.68	527	9.89	51.0	29.3
51	15.72	580	1018	10.00	531	9.90	23.2	13.3

V. Second Hemorrhage (3.22 per cent.) Dec. 23, 1902–Jan. 12, 1903

Day No.	Body-weight.	Volume.	Specific gravity.	Nitrogen.	Period average Volume.	Period average Nitrogen.	Fresh.	Dry.
52	15.18	428	1014	5.58	428	5.58	30.3	19.1
53	15.09	590	1027	13.51	509	9.55	...	...
54	14.92	579	1024	13.06	532	10.72	30.6	16.8
55	14.76	620	1020	11.62	554	10.94	57.8	37.7
56	14.76	478	1026	11.89	539	11.13	26.5	18.3
57	14.76	447	1024	10.27	524	10.99	18.4	11.1
58	14.77	534	1024	13.19	525	11.30	27.8	14.7
59	14.77	482	1022	10.93	520	11.26	41.5	20.7
60	14.78	415	1018	7.02	508	10.78	48.7	24.5
61	14.75	566	1023	11.77	514	10.88	24.3	16.7
62	14.70	598	1019	10.29	521	10.83	33.5	16.9
63	14.64	600	1020	11.47	528	10.88	31.8	16.8
64	14.56	534	1020	10.33	529	10.84	69.0	37.7
65	14.44	620	1019	10.97	535	10.85	...	...
66	14.46	468	1020	9.48	531	10.76	35.5	17.5
67	14.45	546	1021	10.97	532	10.77	69.1	35.9
68	14.43	522	1019	9.61	531	10.70	...	...
69	14.45	510	1020	9.84	530	10.65	48.9	26.3
70	14.38	542	1019	9.72	531	10.61	33.5	21.0
71	14.40	518	1018	9.22	530	10.54	37.8	19.8
72	14.42	534	1018	9.17	530	10.47	103.8	46.1

TABLE XII (*Continued*)

VI. Third Hemorrhage (3.51 per cent.) Jan. 13–19, 1903

Day No.	Body-weight.	Urine.					Feces.	
		Volume.	Specific gravity.	Nitrogen.	Period average to date.		Weight.	
					Volume.	Nitrogen.	Fresh.	Dry.
	kilos	cc.		grams	cc.	grams	grams	grams
73	13.76	460	1018	7.91	460	7.91	...	...
74	13.80	475	1026	11.55	468	9.73	...	...
75	13.70	624	1021	13.01	520	10.82	47.5	23.0
76	13.76	394	1023	9.03	488	10.38	42.3	21.7
77	13.82	412	1024	10.44	473	10.39	57.8	28.0
78	13.80	484	1024	10.96	475	10.48	103.9	38.5
79	13.77	488	1018	8.33	477	10.18	56.5	19.7

VII. Fourth Hemorrhage (3.26 per cent.) Jan. 20–23, 1903

80	13.35	463	1018	8.88	463	8.88	...	...
81	13.36	518	1033	13.92	490	11.40	...	...
82	13.04	770	1022	17.14	584	13.31	29.5	15.9
83	12.90	464	1024	11.75	554	12.92	134.5	59.6

VIII. Fifth Hemorrhage (2.46 per cent.) Jan. 24–25, 1903

84	12.63	455	1026	11.28	....	....	....	....
85	....	14	1036	Death occurred at the end of the second hour.				

TABLE XIII

RELATION BETWEEN TOTAL NITROGEN AND VOLUME OF URINE.

Period.	Date.	No. of days.	Average Nitrogen (grams)	Average volume. cc.	Ratio. (N : V)
Preliminary experiment....	Nov. 2–13 1902	12	8.74	489	1:55.9
After first hemorrhage ..... (2.93 per cent.)	Nov. 14–18	5	10.37	475	1:45.8
Preliminary to Anaesthesia Experiment .... (Dog in nitrogen equil.)	Nov. 25–29	5	9.52	519	1:54.5
First four days of Anaesthesia experiment........... (Control experim't No. 1)	Nov. 30–Dec. 3	4	8.54	501	1:58.7
Last four days of Anaesthesia experiment........... (Dog in nitrogen equilibrium)	Dec. 6–9	4	9.16	563	1:61.5
First five days of Anaesthesia-operation experiment. (Control experim't No. 2)	Dec. 10–14	5	9.96	541	1:54.3
Preliminary to second hemorrhage .... (Dog in nitrogen equil.)	Dec. 19–22	4	9.49	529	1:55.7
After second hemorrhage... (3.22 per cent.)	Dec. 23–29	7	11.30	525	1:46.5
Preliminary to third hemorrhage................ (Dog in nitrogen equil.)	Jan. 8–12 1903	5	9.51	525	1:55.2
After third hemorrhage .... (3.51 per cent.)	Jan. 13–15	3	10.82	520	1:48.1
After fourth hemorrhage ... (3.26 per cent.)	Jan. 20–21	2	11.40	490	1:43.0
After fifth hemorrhage ..... (2.46 per cent.)	Jan. 24	1	11.28	455	1:40.3

TABLE XIV

NITROGEN CONTENT OF COMPOSITE URINE SAMPLES.

Series of experiments.	Experiment.	No. of days.	Nitrogen (grams).		
			Content of composite urine sample.	Total content of daily samples.	Daily variation.
First Series.	Preliminary	12	104.30	104.84	0.045
	First hemorrhage	16	152.31	152.68	0.023
	Anaesthesia	10	89.48	89.57	0.009
	Anaesthesia-operation	13	130.32	128.70	0.125
	Second hemorrhage ..	21	220.48	219.91	0.027
	Third hemorrhage	7	70.54	71.23	0.098
	Fourth hemorrhage...	4	51.16	51.69	0.142
	Total	83	**818.59**	**818.62**	**0.03**[1]
Second Series.	Preliminary..........	9	69.92	69.57	0.039
	Anaesthesia-operation	9	78.82	79.11	0.032
	Hemorrhage	5	46.82	47.34	0.104
	Total	23	195.56	196.02	0.46

1 This variation of but 0.03 gram of nitrogen for a period of 83 days is very striking.

TABLE XV

DAILY DIET (SECOND SERIES).

Constituent of the diet.	Amount in grams.	Nitrogen.		Sulphur.		Phosphorus.	
		Per cent.	Grams.	Per cent.	Grams.	Per cent.	Grams.
Beef	200	3.759	7.518	0.288	0.576	0.220	0.440
Cracker dust	52	1.55	0.806	0.1318	0.069	0.1345	0.070
Lard	15	0.028	0.004	0.03	0.004	0.085	0.013
Bone ash	8	0.026	0.002	0.06	0.005	17.79	1.423
Water	375	....	....	....	....	....	....
Total	650	....	8.33	....	0.654	....	1.946

TABLE XVI.—SUMMARY OF NITROGEN BALANCES.

JUNE 2–24, 1903

Experiment.	Date.	Days.	Income (grams). Diet. Nitrogen. Day.	Income (grams). Diet. Nitrogen. Period.	Outgo (grams). Urine. Nitrogen. Day.	Urine. Nitrogen. Period.	Feces. Nitrogen. Day.	Feces. Nitrogen. Period.	Hair. Nitrogen. Day.	Hair. Nitrogen. Period.	Washings. Nitrogen. Day.	Washings. Nitrogen. Period.	Total. Nitrogen. Day.	Total. Nitrogen. Period.	Gain or Loss. Day.	Gain or Loss. Period.
Preliminary...	June 2–10 1903	9	8.33	74.97	7.73	69.57	0.49	4.42	0.11	0.98	0.10	0.88	8.43	75.85	— 0.10	— 0.88
Before anaesthesia-operation........	June 8–10	3	8.33	24.99	7.59	22.77	0.49	1.47	0.11	0.33	0.10	0.30	8.29	24.87	— 0.04	— 0.12
After anaesthesia-operation........	June 11–16	6	8.33	49.98	9.14	54.84	0.43	2.58	0.12	c.72	0.08	0.48	9.77	58.62	— 1.44	— 8.64
After anaesthesia-operation........	June 11–19	9	8.33	74.97	8.79	79.11	0.43	3.87	0.12	1.08	0.08	0.72	9.42	84.78	— 1.09	— 9.81
Before hemorrhage......	June 17–19	3	8.33	24.99	8.08	24.24	0.43	1.29	0.12	0.36	0.08	0.24	8.71	26.13	— 0.38	— 1.14
After hemorrhage....... (3.11 per cent.)	June 20–24	5	8.33	41.65	9.47	47.34	0.46	2.32	0.11	0.55	0.17	0.87	10.21	51.08	— 1.88	— 9.43

TABLE XVII

Daily Data of the Second Series of Experiments.

I. Preliminary Experiment, June 2–10, 1903

Day No.	Body-weight.	Urine.					Feces.	
		Volume.	Specific gravity.	Nitrogen.	Period average to date.		Weight.	
					Volume.	Nitrogen.	Fresh.	Dry.
	kilos	cc.		grams	cc.	grams	grams	grams
1	11.85	390	1016	7.63	390	7.63	22.8	15.8
2	11.80	415	1018	6.99	403	7.31	...	...
3	11.82	388	1020	7.58	398	7.40	50.2	29.3
4	11.70	485	1020	9.65	419	7.96	...	...
5	11.76	344	1017	5.31	404	7.43	...	...
6	11.60	515	1018	9.63	423	7.80	40.3	30.8
7	11.57	402	1019	8.14	420	7.85	34.2	21.4
8	11.63	298	1018	5.52	405	7.56	40.0	23.5
9	11.68	452	1020	9.12	410	7.73	41.5	24.3

II. Anaesthesia—operation, June 11–19, 1903

Day No.	Body-weight.	Volume.	Specific gravity.	Nitrogen.	Period average Volume.	Period average Nitrogen.	Feces Fresh.	Feces Dry.
10	11.40	450	1019	8.56	450	8.56	54.8	31.8
11	11.30	560	1019	9.46	505	9.01	...	...
12	11.28	484	1018	9.33	498	9.12	22.5	17.9
13	11.24	432	1019	8.66	482	9.00	...	...
14	11.26	422	1016	6.31	470	8.46	57.5	28.5
15	11.10	544	1023	12.55	482	9.14	...	...
16	11.06	383	1018	7.11	468	8.85	46.2	28.8
17	11.03	404	1020	8.00	460	8.75	29.1	19.1
18	11.00	480	1018	9.13	462	8.79	...	...

III. Hemorrhage (3.11 per cent.) June 20–24, 1903

Day No.	Body-weight.	Volume.	Specific gravity.	Nitrogen.	Period average Volume.	Period average Nitrogen.	Feces Fresh.	Feces Dry.
19	10.47	442	1020	8.96	442	8.96	37.6	26.5
20	10.63	323	1028	9.59	383	9.28	...	...
21	10.60	418	1019	8.51	394	9.02	37.5	28.3
22	10.58	445	1023	9.94	407	9.25	...	...
23	10.48	503	1021	10.34	426	9.47	41.0	19.8

TABLE XVIII.—SUMMARY OF SULPHUR AND PHOSPHORUS BALANCES.

JUNE 2–24, 1903

SULPHUR

Experiment.	Date.	Days.	Income (grams). Diet. Sulphur.		Outgo (grams). Urine. Sulphur.		Feces. Sulphur.		Hair. Sulphur.		Washings. Sulphur.		Total. Sulphur.		Gain or Loss.	
			Day.	Period.	Day.	Period.	Day.	Period.	Day.	Period.	Day.	Period.	Day.	Period.	Day.	Period.
Preliminary...	June 2–10 1903	9	0.654	5.886	0.474	4.270	0.148	1.334	0.022	0.210	0.009	0.079	0.653	5.893	— 0.001	— 0.007
Anaesthesia—operation...	June 11–19	9	0.654	5.886	0.529	4.766	0.142	1.285	0.027	0.247	0.009	0.084	0.707	6.382	— 0.053	— 0.495
Hemorrhage.. (3.11 per cent.)	June 20–24	5	0.654	3.270	0.586	2.928	0.145	0.723	0.025	0.128	0.008	0.042	0.764	3.821	— 0.110	— 0.551

PHOSPHORUS

Experiment.	Date.	Days.	Income (grams) Diet. Phosphorus.		Outgo (grams). Feces. Phosphorus.		Urine. Phosphorus.		Hair. Phosphorus.		Washings. Phosphorus.		Total. Phosphorus.		Gain or Loss.	
			Day.	Period.	Day.	Period.	Day.	Period.	Day.	Period.	Day.	Period.	Day.	Period.	Day.	Period.
Preliminary...	June 2–10 1903	9	1.946	17.514	1.554	13.984	0.403	3.624	0.011	0.099	0.008	0.072	1.976	17.779	— 0.030	— 0.265
Anaesthesia—operation...	June 11–19	9	1.946	17.514	1.475	13.276	0.475	4.276	0.012	0.105	0.009	0.079	1.971	17.736	— 0.025	— 0.222
Hemorrhage.. (3.11 per cent.)	June 20–24	5	1.946	9.730	1.452	7.259	0.492	2.461	0.010	0.051	0.009	0.045	1.963	9.816	— 0.017	— 0.086

TABLE XIX.—TABLE OF SUMMARIES (First Series).

Experiment.	Day of maximum urine volume.	Daily increase in Nitrogen excretion.					Daily decrease in nitrogen excretion due to A. (grams)	Sulphur excretion.		Phosphorus excretion.	
		Due to H., O., A.[1] (grams)	Due to H., O. (grams)	Due to H. (grams)	Due to O., A. (grams)	Due to O. (grams)		Daily increase. (grams)	Daily decrease. (grams)	Daily increase. (grams)	Daily decrease. (grams)
First hemorrhage .... (2.93 per cent.)	16	1.257	2.194	0.488	.....	.....	.....	0.023	.....	.....	0.123
Anaesthesia	1	.....	.....	.....	.....	.....	0.937	.....	0.128	0.108	.....
Anaesthesia-operation	1	.....	.....	.....	0.769	1.706	.....	0.119	.....	.....	0.148
Second hemorrhage .. (3.22 per cent.)	4	1.799	2.736	1.030	.....	.....	.....	0.180	.....	.....	0.163
Third hemorrhage ... (3.51 per cent.)	3	1.248	2.185	0.479	.....	.....	.....	0.229	.....	.....	0.065
Fourth hemorrhage .. (3.26 per cent.)	3	3.275	4.212	2.506	.....	.....	.....	0.348	.....	0.180	.....

[1] Abbreviations as follows:
H. = Hemorrhage.
O. = Operation.
A. = Anaesthesia.